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A Medical Device to prevent Sudden Death in Epilepsy: From the Bench to the Market

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A Medical Device to prevent Sudden Death in Epilepsy: From the Bench to the Market

Dissertation

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O homem não nasceu para trabalhar,

nasceu para criar, para ser o tal poeta à solta.

Agostinho da Silva

Para a minha querida Lídia

Para os meus orgulhosos Papá e Mamã

Para a nova e mais querida geração:

Carlota, António and Tomás

Gratitude

As *God wants, the man dream and the work is born*, this thesis was seeded ten years ago. In a serendipity moment, it was revealed to me that the human body is designed in its physiology to endure an unexpected event, and the impairment of this resilience could be the cause behind sudden unexpected death in epilepsy.

As I am grateful to God who planted this idea in my mind, I am also grateful to my wife Lídia who nurtured it until now. Thank you for supporting me by heart during those arid and discouraging years when the scalding sun of multiple rejections has almost stopped its germination. Lidia, your faith and patience kept me walking through these last years. Thank you for taking care of everything and everyone during those eternal hours and countless weekends when I was reading, writing, meeting, traveling, living abroad. Thank you for insisting for me to wait to talk with Professor Emilio, thank you to bring our kids to Burgos, thank you for your courage to see in first person why this thesis is meaningful. Thank you for your love, kindness and enthusiasm, those were my strengths.

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Abstract

Sudden Unexpected Death in Epilepsy (SUDEP) represents the most catastrophic and least understood consequence of drug-resistant epilepsy. While technological advances have enabled the development of seizure detection tools, very few medical devices explicitly target SUDEP prevention, and even fewer are co-designed with persons with epilepsy (PWEs) and caregivers (CGs). This thesis investigates how a user-centered, ethically grounded, and participatory approach can inform the development of artificial intelligence-driven, closed-loop medical devices for SUDEP risk reduction. Grounded in the NEUROSENSE project, this research combines a systematic literature review, a cross-sectional survey, and qualitative studies with PWE and CGs to examine user attitudes, ethical concerns, and design preferences. Findings reveal a critical gap in early-stage user involvement in current medical device innovation, particularly during concept and design phases. By engaging stakeholders from the project's inception through iterative co-design workshops, this thesis demonstrates that it is feasible to integrate user needs while maintaining intellectual property protection. Key user priorities—such as comfort, discretion, emotional safety, and adaptability—were embedded into a prototype whose development was directly shaped by stakeholder input. This work offers a scalable framework for medical device innovation that bridges technical excellence with emotional and ethical acceptability. It contributes to translational research by moving from biomarker identification at the bench to a participatory design process that lays the foundation for future clinical and market integration.

KEYWORDS

Epilepsy; SUDEP; Medical Device Development; User-Centered Design; AI-Driven Devices; Participatory Design; Closed-Loop Systems; Co-Creation; Intellectual Property; Digital Health; Translational Research; Healthcare Innovation; Persons with Epilepsy; Caregivers.

Resumo

A morte súbita inesperada em epilepsia representa a consequência mais catastrófica e menos compreendida da epilepsia farmacorresistente. Embora os avanços tecnológicos tenham possibilitado o desenvolvimento de ferramentas para deteção de convulsões epilépticas, poucos dispositivos médicos têm como foco explícito a prevenção de SUDEP, e ainda menos são co-desenhados com pessoas com epilepsia e cuidadores. Esta tese investiga como uma abordagem centrada no utilizador, fundamentada eticamente e participativa pode orientar o desenvolvimento de dispositivos médicos de circuito fechado, baseados em inteligência artificial, para a redução do risco de morte súbita inesperada em epilepsia. Inserida no projeto NEUROSENSE, esta investigação combina uma revisão sistemática da literatura, um inquérito transversal e estudos qualitativos com pessoas com epilepsia e cuidadores, para examinar atitudes, preocupações éticas e preferências de design. Os resultados revelam uma lacuna crítica na participação dos utilizadores nas fases iniciais do desenvolvimento de dispositivos médicos, particularmente durante a conceção e o design. Ao envolver as partes interessadas desde o início do projeto, através de workshops interativos de co-design, esta tese demonstra que é possível integrar as necessidades dos utilizadores sem comprometer a proteção da propriedade intelectual. Prioridades-chave como conforto, discrição, segurança emocional e adaptabilidade foram incorporadas no protótipo, cujo desenvolvimento foi moldado diretamente pelo contributo dos utilizadores. Este trabalho oferece um modelo escalável de inovação em dispositivos médicos, que concilia excelência técnica com aceitabilidade emocional e ética. Contribui para a investigação translacional ao evoluir da identificação de biomarcadores no laboratório para um processo de design participativo que fundamenta a futura integração clínica e comercial.

PALAVRAS-CHAVE

Epilepsia; SUDEP; Desenvolvimento de Dispositivos Médicos; Design Centrado no Utilizador; Dispositivos com Inteligência Artificial; Co-Criação; Sistemas de Circuito Fechado; Inovação em Saúde; Participação de partes interessadas; Propriedade Intelectual; Saúde Digital; Investigação Translacional; Pessoas com Epilepsia; Cuidadores

Table of Contents

Index of Figures

Index of Tables

Chapter 2. User involvement in the design and development of medical devices in epilepsy: A systematic review

Chapter 3. Towards user-centered design of medical devices for SUDEP prediction and prevention: Insights from persons with epilepsy and caregivers

Chapter 5. Supplementary Data

List of Abbreviations and Acronyms

AI	Artificial Intelligence
AI-CLD	Artificial Intelligence-Driven Closed Loop Device
CREER	Centro De Referencia Estatal De Atención A Personas Con Enfermedades Raras Y Sus Familias
CG	Caregiver
EEG	Electroencephalography
EISMEA	European Innovation Council And Smes Executive Agency
EMA	European Medicines Agencies
FCT	Fundação Para A Ciência E A Tecnologia
FDA	Food And Drug Administration
ILAE	International League Against Epilepsy
ISF	Interstitial Fluid
i3S	Instituto De Investigação E Inovação Em Saúde Da Universidade Do Porto
GDPR	General Data Protection Regulation
GTCS	Generalized Tonic-Clonic Seizures
HP	Healthcare Professional
LPCE	Liga Portuguesa Contra A Epilepsia
MDD	Medical Device Development
PAB	Patient Advisory Board
PWE	Person With Epilepsy
PRISMA	Preferred Reporting Items For Systematic Reviews And Meta-Analyses
PROSPERO	International Prospective Register Of Systematic Reviews
SPSS	Software Package For Social Sciences
SUDEP	Sudden Unexpected Death In Epilepsy
UCD	User-Centered Design
VNS	Vagus Nerve Stimulators
WHO	World Health Organization

1.

Introduction

1. Background

Epilepsy is the fourth most common neurological disorder after Alzheimer disease, migraine, and stroke, affecting over 65 million people worldwide with a lifetime prevalence of around 7.6 per 1,000 people [1]. Accordingly with the International League Against Epilepsy (ILAE), epilepsy is defined as a disease of the brain that results in at least two unprovoked seizures at least 24 hours apart. A diagnosis may also be made after one unprovoked seizure if there is a high chance (>60%) of having another seizure within the next 10 years or if the patient has an epilepsy syndrome [2]. Although epilepsy is characterized by epileptic seizures (a transient occurrence of signs and/or symptoms due to abnormal or synchronous neuronal activity in the brain), it can include a wide range of difficulties in cognition, psychiatric status, and social adaptive functioning, with caregiver and sibling quality of life often negatively affected [3] [4]. The burden of comorbidity in people with epilepsy is high, with several diseases and conditions, including depression, anxiety, dementia, migraines, heart disease, peptic ulcers and arthritis being more common in people with epilepsy than in the general population. Therefore, epilepsy has been progressively recognized as a condition reaching well beyond seizures, and today it can be properly considered as a multifaced spectrum disorder [5]. Despite the availability of over 30 antiseizure medications, approximately 30–40% of persons with epilepsy have drug resistant epilepsy. This hinders optimal seizure control and increases the vulnerability to serious complications [6].

Among these, sudden unexpected death in epilepsy (SUDEP) is considered to be the most catastrophic complication of epilepsy and poses a substantial public health burden [7]. Among deaths directly attributable to epilepsy or seizures, SUDEP is the leading cause accounting for 7–17% of deaths among the general population with epilepsy and estimated 50% of deaths among patients with refractory epilepsy [8]. Although SUDEP incidence is lower in children than in adults, SUDEP occurs in pediatric epilepsies, especially in genetic developmental and epileptic encephalopathies [9]. SUDEP is defined as a sudden, unexpected, witnessed or unwitnessed, nontraumatic and non-drowning death in patients with epilepsy, with or without evidence for a seizure and excluding documented status epilepticus, in which postmortem examination does not reveal a toxicologic or anatomic cause of death [10]. The exact pathophysiology mechanisms are not known, but postictal cardiac, respiratory, and brainstem dysfunctions are implicated [11]. Still, epidemiological data allows to identify chronic refractory epilepsy, in particular nocturnal generalized tonic-clonic seizures (GTCS) in prone position as the major risk factor for SUDEP [12].

Although several societies such as the American Epilepsy Society and the American Academy of Neurology have recommended discussing SUDEP with patients and their families [13], [14], clinicians generally avoid SUDEP discussions due to concerns of creating anxiety, often limiting them to high-risk persons with epilepsy (PWE) [15]. Furthermore, some neurologists are also unlikely to discuss SUDEP due to the absence of proven predictive and preventative measures [16]. Despite considerable research, the cause of SUDEP is still largely unknown, and one of the most pressing limitations in advancing SUDEP prevention is the lack of validated biomarkers that could inform risk stratification or guide prevention strategies and intervention studies [17]. In the absence of SUDEP biomarkers, SUDEP prevention efforts primarily focus on seizure control, nocturnal monitoring, and lifestyle modifications. However, these approaches remain insufficient in mitigating risk, as many cases occur unexpectedly, even in individuals receiving optimal medical treatment [18]. This highlights the urgent need for more proactive, technologically enabled approaches for SUDEP prediction and prevention.

Recent years have seen a proliferation of medical devices and digital health tools aimed at detecting seizures and alerting caregivers such as vagus nerve stimulators (VNS), responsive neurostimulation and deep brain stimulation to non-implantable devices such as electroencephalography (EEG)-based systems and non-EEG-based seizure detection wearable devices [19]. These may also be advantageous and effective for detecting nocturnal epileptic seizures, which therefore may reduce the occurrence of SUDEP in epileptic patients, particularly when combined with an automated alarm system or intervention trigger, VNS or automated seizure detection systems [19]. However, these tools have not been explicitly developed or validated for SUDEP prevention, and further studies for the validation of these proposed devices in terms of reliability, safety, accuracy, sensitivity and specificity in detecting and predicting patient-specific seizures are needed [20]. With the rapid development in artificial intelligence, the potential for application these medical devices in SUDEP prediction and prevention offers transformative possibilities.

An innovative avenue in this topic is the development of Artificial Intelligence (AI)-driven closed loop devices — technologies that integrates real-time data acquisition, AI-based predictive modelling, and automated interventions. For example, a system might detect and distinguish a potentially fatal seizure and trigger the delivery of an intervention. In theory, such devices could interrupt the cascade of events leading to SUDEP. Yet the practical deployment of these devices is still nascent, and their design is often driven more by technical feasibility than by user priorities or ethical reflection.

This points to a broader issue in medical device development for epilepsy: the limited involvement of PWE, caregivers, and healthcare professionals. User involvement in the development of epilepsy-related medical devices remains limited, often resulting in products that do not align with the practical needs and preferences of PWEs and CGs. Wearability, comfort, discretion, emotional acceptability, and trust are often afterthoughts, rather than core design criteria.

In applications as time-critical as SUDEP, where stakes are so personal and consequences so dire, user-centered design (UCD) is not merely desirable — it is essential. UCD approaches emphasize iterative engagement with users throughout the development cycle, from bench to the market, preventing usability limiting factors such as device discomfort, aesthetic concerns, and lack of personalization that will ultimately contribute to reduced adherence among users [21]. The development of AI-driven automated interventions must go beyond technical functionality—it must be led by empathy, ethics, and an intimate sense of what matters most to those who will be living with these devices. The idea of a system that might detect a potentially lethal seizure and administer treatment on its own is irresistibly attractive. Yet for those individuals who depend on such technology, the issue is far more complicated. False alarms can mean being woken up abruptly, experiencing unwanted side effects of medication, or living with a constant sense of uncertainty. On the other hand, a failure to detect an event could have catastrophic consequences. These are more than technical problems; they are deep emotional problems that affect people's feelings about whether they can trust a machine to preserve their own lives or the lives of their loved ones.

Consequently, UCD is not just a best practice in this case but a moral obligation. In trying to actually design these systems, an entry point must be developed into how individuals perceive and react to automated decision-making, particularly at their most vulnerable moments. While some will embrace any opportunity for protection, regardless of the additional inconvenience, others may view ubiquitous monitoring as an intrusion into their autonomy or an exacerbation of their anxieties. Ultimately, the success of these devices will not be based on their theoretical underpinnings alone, but on their practical utility in real-world use for real users. Working with the insights of people living with epilepsy and actively integrating their feedback at every stage of the design process is the only way to develop tools that are not just effective, but also meaningful, trustworthy, and embraced by the groups that need them most.

This thesis is positioned at the intersection of epilepsy research, digital health innovation, and participatory design. It explores how SUDEP-targeted devices can be developed not only with technical rigor but with deep engagement from those most affected. By grounding device development in the lived experiences, values, and concerns of users, this work aims to support more effective, ethical, and equitable innovations in SUDEP prevention.

2. Motivation

Recognizing SUDEP as the most catastrophic complication of epilepsy and a substantial public health burden, the American Epilepsy Foundation launched the *SUDEP Challenge* aimed at identifying biomarkers to predict SUDEP. Engagement with this initiative exposed the researcher to the urgent medical need to develop clinically relevant, specific, and sensitive biomarkers of SUDEP that would allow development of a therapeutic intervention for people at high risk for SUDEP or life-threatening seizures.

That experience became the catalyst for what would later become the NEUROSENSE project: a multidisciplinary research initiative aimed at developing intelligent seizure-monitoring and intervention systems. Given the urgency of this unmet need, the NEUROSENSE Project condenses the identification of potential SUDEP biomarkers in preclinical SUDEP animal models, with the assessment in the clinical setting alongside with the engineering group that develops a medical device prototype with a sensor aimed at quantifying these biomarkers. When designing this project, soon the researcher realized that the development of a SUDEP predictive and preventive biomarker would not be translated into an effective therapeutic without involving PWEs and CGs in the co-creative process. As the lead on user research within NEUROSENSE, the researcher was responsible for exploring how PWEs, CGs, and healthcare professionals (HPs) respond to these emerging technologies. The work involved not only gathering user insights but also helping shape the ethical and technical trajectory of the devices themselves. This thesis is the culmination of that effort.

2. Research Gaps and Questions

Despite the growing burden of epilepsy and the tragic toll of SUDEP, there remains a significant innovation gap in technologies that can proactively reduce SUDEP risk. Current devices primarily focus on seizure detection rather than SUDEP prevention, and most are designed without substantial input from PWE or their CGs. Furthermore, AI-based closed-

loop devices — while promising in theory — are in early stages of development and lack comprehensive evaluation from the perspective of those who would use them.

The overarching aim of this thesis is to investigate how PWEs, their CGs, and other stakeholders perceive, evaluate, and respond to medical devices designed to reduce the risk of SUDEP — with a focus on AI-based, closed-loop systems. This aim responds to a pressing gap in current innovation efforts: the disconnect between technological promise and UCD in high-risk neurological care.

The research is guided by the following core questions:

1. To what extent have users been involved in the design and development of medical devices for epilepsy, particularly those targeting SUDEP?

   This question is addressed through a systematic review of existing literature, analyzing patterns of user engagement across the device lifecycle.

2. What are the attitudes, concerns, and design preferences of PWE and CGs regarding wearable devices for SUDEP prevention?

   A cross-sectional survey explores how prospective users evaluate such technologies in terms of functionality, usability, aesthetics, and emotional burden.

3. How do users perceive the ethical and practical dimensions of AI-based closed-loop systems for seizure intervention?

   Focus groups and interviews within the NEUROSENSE project examine stakeholder reactions to autonomous intervention, risk communication, trust, and safety.

4. What design principles and strategies can be derived to support user acceptance and long-term adoption of such technologies?

   Insights from across the studies are synthesized to inform both theoretical understanding and practical guidance for the development of SUDEP-targeted devices.

By addressing these questions, the thesis aims to contribute to three key domains:

- Medical innovation — by identifying UCD principles for high-risk neurological technologies.

- Epilepsy care — by amplifying PWE and CG voices in the development of solutions to reduce SUDEP.
- Science and technology studies — by offering an empirically grounded case study of how emerging technologies are negotiated at the intersection of ethics, affect, and design.

In doing so, this research seeks to reframe the process of medical device development in epilepsy — not just as a technical endeavor, but as a collaborative, value-laden practice that must engage with the lived realities of those most affected.

3. Methodological Approach

To comprehensively explore this multidimensional topic, the thesis adopts a mixed methods design, drawing on both quantitative and qualitative data to address its research questions from multiple angles.

The methodological progression follows three major phases:

1. Systematic Review – The first study surveys existing literature on SUDEP-related technologies, examining how and when users have been involved in their design and development. This maps the current state of practice and identifies common limitations in stakeholder engagement.
2. Survey Study – The second study engages directly with PWEs and their CGs via an online questionnaire. It captures attitudes toward hypothetical SUDEP-prevention devices, exploring perceptions of usefulness, intrusiveness, emotional acceptability, and trust.
3. Qualitative Study – The third study is a qualitative exploration embedded within the NEUROSENSE project. Using focus groups and interviews, it examines reactions to a specific AI-based, closed-loop system for seizure intervention, with attention to ethical, practical, and emotional themes.

This sequence — from literature synthesis to stakeholder survey to embedded qualitative work — reflects a real-world bench-to-market innovation pathway. It allows the research to move from diagnosing systemic gaps, to eliciting user needs, to testing perceptions of an actual, in-development technology.

4. Thesis Outline

This thesis is closely embedded in the **NEUROSENSE project**, a European research initiative focused on the development of intelligent, closed-loop devices for seizure intervention and SUDEP risk reduction. My role within NEUROSENSE involved leading the user research component, helping to ensure that real-world stakeholder needs shaped device features, design logic, and risk communication strategies.

The thesis is structured as follows:

- **Chapter 2 – Systematic Review**

  Reviews the state of user engagement in medical device development for epilepsy. It highlights the dominance of engineering-led approaches and identifies patterns in how (and when) users are involved — or excluded — from the innovation process. The author was responsible for conceptualization, study design, and search strategy for this review [22].

- **Chapter 3 – Survey Study**

  Presents a cross-sectional study involving PWEs and CGs, exploring their preferences and concerns regarding a hypothetical wearable device for SUDEP prevention. The results reveal tensions between technological promise and lived experience, and they identify key design priorities such as comfort, discretion, reliability, and emotional impact. The author carried out the survey study and played a lead role in data curation and formal analysis. [23].

- **Chapter 4 – Qualitative Study**

  Analyzes data from focus groups and interviews exploring perceptions of AI-based closed-loop devices. The study addresses user attitudes toward autonomy, safety, trust, and control, providing valuable guidance for future development within NEUROSENSE and similar projects. The author was responsible for conceptualization and conduction of the focus groups and played a lead role in data curation and formal analysis.

- **Chapter 5 – Conclusion**

  Summarizes the key contributions of the thesis, reflects on its limitations, and outlines recommendations for future research, policy, and practice. It emphasizes

that reducing SUDEP risk requires not just smarter technologies, but deeper collaboration with those who live with epilepsy every day.

Through this structure, the thesis moves from prediction to design to deployment — offering both a critique of current practices and a roadmap for more inclusive, impactful innovation in epilepsy care.

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2.

User involvement in the design and development of medical devices in epilepsy: A systematic review

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Keywords

Epilepsy, Medical Device Design, Medical Devices, User involvement

Abstract

Objective: This systematic review aims to describe the involvement of persons with epilepsy (PWE), healthcare professionals (HP) and caregivers (CG) in the design and development of medical devices is epilepsy.

Methods: A systematic review was conducted, adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Eligibility criteria included peer-reviewed research focusing on medical devices for epilepsy management, involving users (PWE, CG, and HP) during the medical device development (MDD) process. Searches were performed on PubMed, Web of Science, and Scopus, and a total of 55 relevant articles were identified and reviewed.

Results: From 1999 to 2023, there was a gradual increase in the number of publications related to user involvement in epilepsy MDD, highlighting the growing interest in this field. The medical devices involved in these studies encompassed a range of seizure detection tools, healthcare information systems, vagus nerve stimulation (VNS) and electroencephalogram (EEG) technologies reflecting the emphasis on seizure detection, prediction, and prevention. PWE and CG were the primary users involved, underscoring the importance of their perspectives. Surveys, usability testing, interviews, and focus groups were the methods used for capturing user perspectives. User involvement occurs in four out of the five stages of MDD, with production being the exception. Significance: User involvement in the MDD process for epilepsy management is an emerging area of interest holding a significant promise for improving device quality and patient outcomes. This review highlights the need for broader and more effective user involvement, as it currently lags in the development of commercially available medical devices for epilepsy management. Future research should explore the benefits and barriers of user involvement to enhance medical device technologies for epilepsy.

Plain Language Summary: This review covers studies that have involved users in the development process of medical devices for epilepsy. The studies reported here have focused on getting input from people with epilepsy, their caregivers, and healthcare providers. These devices include tools for detecting seizures, stimulating nerves, and tracking brain activity. Most user feedback was gathered through surveys, usability tests,

interviews, and focus groups. Users were involved in nearly every stage of device development except production. The review highlights that involving users can improve device quality and patient outcomes, but more effective involvement is needed in commercial device development. Future research should focus on the benefits and challenges of user involvement.

1. Introduction

Epilepsy impacts approximately 70 million individuals and 30 % of them do not respond to current treatments to control their seizures [1]. Accurately anticipating the onset of seizures and managing them can assist PWE in avoiding self-injury and potentially enhance their overall well-being. Seizure detection and, more recently, seizure forecasting are critical areas of clinical advancement in epilepsy. The progress in these areas has been driven by developments in medical devices, which have the potential to optimize seizure control and prevent seizure-related morbidity and mortality in individuals with epilepsy [2].

Medical devices used in epilepsy range from implantable devices such as vagus nerve stimulators, responsive neurostimulation and deep brain stimulation to non-implantable devices such as electroencephalography (EEG) based systems and non-EEG based seizure detection wearable devices [1]. Regardless of the type of medical device, the ultimate goal is to develop devices that meet the needs of end-users (PWE, CGs and HP), improve disease outcomes, and enhance the overall quality of life of individuals with epilepsy.

Medical device manufacturers create life-changing innovations through the collaborative expertise of various disciplines, including engineering, manufacturing, clinical, regulatory, marketing, sales, and business specialists. While cutting-edge technology advancement in medical device design is absolutely vital, it is the overall experience (cognitive and emotional) that impacts the daily life of the patient and CG [3]. In recent years, there has been a growing recognition of the importance of user involvement in MDD in general [4], and specifically for epilepsy [5]. In epilepsy, user involvement refers to the active participation of PWE, CGs, HP and other stakeholders in the design and development of medical devices. Understanding and incorporating users' needs, preferences, and feedback into the MDD process can help to ensure that the device is effective, safe, and well-received by the intended users. User involvement can take various forms, including needs assessment, usability testing, co-creation and co-design [6]. User-centred design is a critical factor in the design and development of medical devices. Specifically, considering user needs during the early stages of device conceptualization and throughout the subsequent development process can yield substantial benefits. This approach can improve patient safety, increase compliance with treatment regimens, and enhance health outcomes [7]. Additionally, user-centred design promotes higher levels of user satisfaction, and it can lead

to a reduction in device development time by identifying and addressing usability issues prior to launch. This, in turn, can help to avoid costly design changes and product recalls, which can have significant financial and reputational implications for device manufacturers [8]. Therefore, successful medical device innovation requires investigation of end-user and broader stakeholder contexts and incorporation of those context-specific needs into design processes [9]. Despite the initial promise that user involvement in medical device design and development for epilepsy holds, there is widespread scepticism regarding its effectiveness within the scientific, medical, and general communities, leaving important choices and questions open for debate, namely: (i) who should be involved, (ii) at which stages should they be involved, (iii) which participatory methods are most suitable and (iv) what topics are to be discussed with end users during development. Therefore, we conducted a systematic review to explore the practice of user involvement in the design and development of medical devices for epilepsy, aiming to provide valuable insights into the role of user involvement in this context and inform future research and practice in this area. Descriptive statistics and qualitative thematic analysis were used for analysing the data, which were divided into different themes, i.e., types of medical devices developed and assessed; types of medical device users involved; extent of user involvement by different stages of the MDD cycle; and methods used for capturing users' perspectives.

2. Methods

The present systematic literature review was performed to identify and extract all currently available literature related to user involvement in medical devices or technology utilized in the monitoring, treatment and/or management of epilepsy.

2.1. Protocol and registration

This systematic review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [10], and was prospectively registered on the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42023490599).

2.2. Eligibility Criteria

Publications inclusion and eligibility for short-listing criteria encompassed (a) peer-reviewed original research, (b) targeted only at medical devices according to World Health Organization (WHO)'s definition [11] with application for epilepsy management and (c) indicating user (PWE, CG and HP) involvement during these products' development lifecycle.

Original publications were excluded if presenting any of the following characteristics: the wrong population (i.e., non-human population); the wrong intervention (i.e., medical

devices used for other purposes rather than epilepsy management); the wrong outcome (i.e., there were no epilepsy or seizure diagnosis, management, or treatment outcomes); publication not available in the English language; publications not in full publication. All studies published up to 30 November 2023 were included with no other time limitations.

2.3. Search strategy

Search strings related to medical devices, users' (PWE, CG and HP) involvement and epilepsy were developed. Thus, the search term ("epilepsy") was searched in combination with the following search strings: ("device users" OR "end-users" OR "medical devices" OR "medical device users" OR "needs assessment" OR "new medical technology" OR "user centered product" OR "user criteria" OR "user input" OR "user interests" OR "user involvement" OR "user needs" OR "user needs assessment" OR "user needs research" OR "user participation" OR "user perceptions" OR "user perspective" OR "user requirements" OR "user requirements elicitation" OR "user studies" or "user survey" OR "user-based" OR "wearable device" OR "device" and "acceptability" OR ("device" AND "usability") OR ("device" AND "satisfaction") OR ("device" AND "patient views")). The Boolean operator AND was used to link the search term with the respective search strings on all databases. Three databases were used from database inception on 30 November 2023: PubMed, Web of Science and Scopus. All searches were performed based on the title, abstract and keyword in all databases. Articles were first screened through their titles and abstracts before proceeding with the full-text screening of relevant articles. The search criteria and keywords were arrived at through consensus with all researchers. Hand searching, personal collections (unpublished studies, conference abstracts, grey literature, or other resources that researchers have accumulated through personal networks or professional contacts) and exploding references (reviewing the reference lists of relevant articles to identify additional studies that may not have been captured through our primary search strategy) were also used to augment the results.

2.4. Selection Process

Database search results were imported into EndNote (EndNote x9; Clarivate, Philadelphia, PA, USA), and duplicates were removed. Results were then exported to an Excel spreadsheet for title, abstract, and full-text screening. Study selection, data extraction and assessment of study quality followed the Standards for Reporting Qualitative Research [12]. No assumptions were made during the selection to reduce the risk of bias. Each paper was screened and discussed by two independent reviewers (JF, RP). Disagreements were resolved by a third independent researcher (CC).

2.5. Data collection and analysis

Data was extracted using a data-extraction form (Table S1) developed for the review [13]. Data extracted included: (1) author details, (2) year of publication, (3) country of study, (4) type of medical device, (5) method/tool/approach, (6) users and (7) product development stages. Since there is no standard framework to describe the MDD stages [14], for data extraction purposes, the medical device lifecycle was divided into five stages: 1- Concept; 2- Design; 3-Testing and Trials; 4- Production; 5-Deployment. The classification of medical device lifecycle stages was carried out based on the product lifecycle reported in the literature (Table 2.1 adapted from Shah and Robinson (15)).

Table 2.1 – Product Lifecycle Stages (Adapted from Shah and Robinson (15))

Medical Device Lifecycle Stage	Details
Concept	Starts with idea generation and includes technical, financial, and commercial assessment
Design	Involves product development process from (re)design to prototype development
Testing and trials	Starts with prototype testing in-house and includes trials in the real field
Production	Includes production on large scale supported by business and commercial rationale
Deployment	Includes product marketing, launch, and use in the real field

3. Results

The study workflow and paper selection process is illustrated in Figure 2.1. Following the inclusion criteria review, 55 publications [17-71] were included, and 109 were excluded (see Figure 2.1 for PRISMA flow chart).

Seventeen of the 55 included publications were from the United States, 7 from the United Kingdom, 6 from Canada, 5 from Denmark, 4 from The Netherlands, 3 from Germany and 3 from South Korea and 1 from Sweden, 1 from Mexico, 1 from France, 1 from Italy and 1 from Belgium. Five studies were of multiple origin (Table S2).

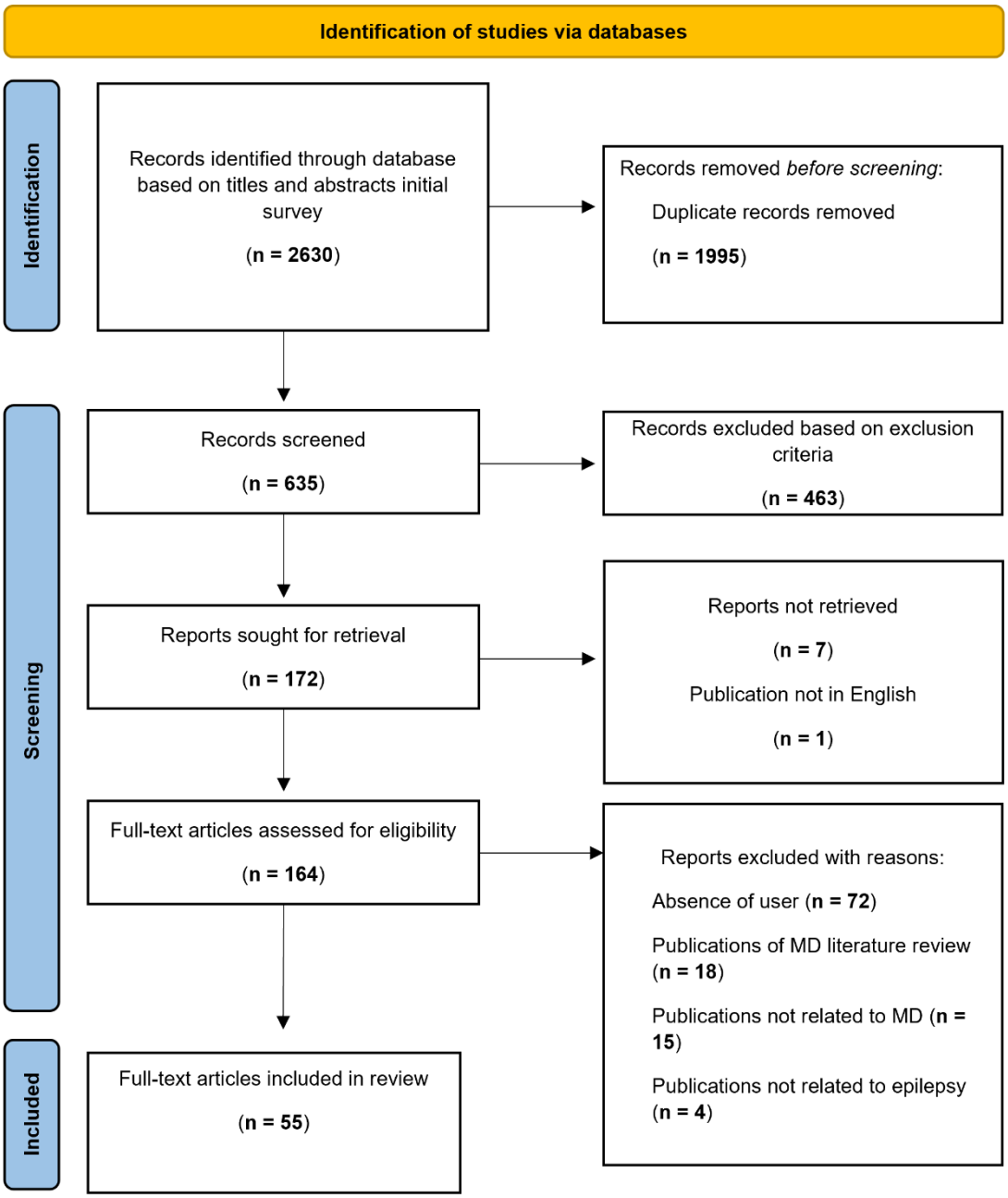

Figure 2.1 – PRISMA Flowchart adopted for the present systematic review

Across the years, we find that user involvement in MDD is becoming more frequent. Figure 2.2 shows the number of papers published per year and the total accumulated number of publications over time since the inaugural paper by Hufford, R.L. and P.M. (16).

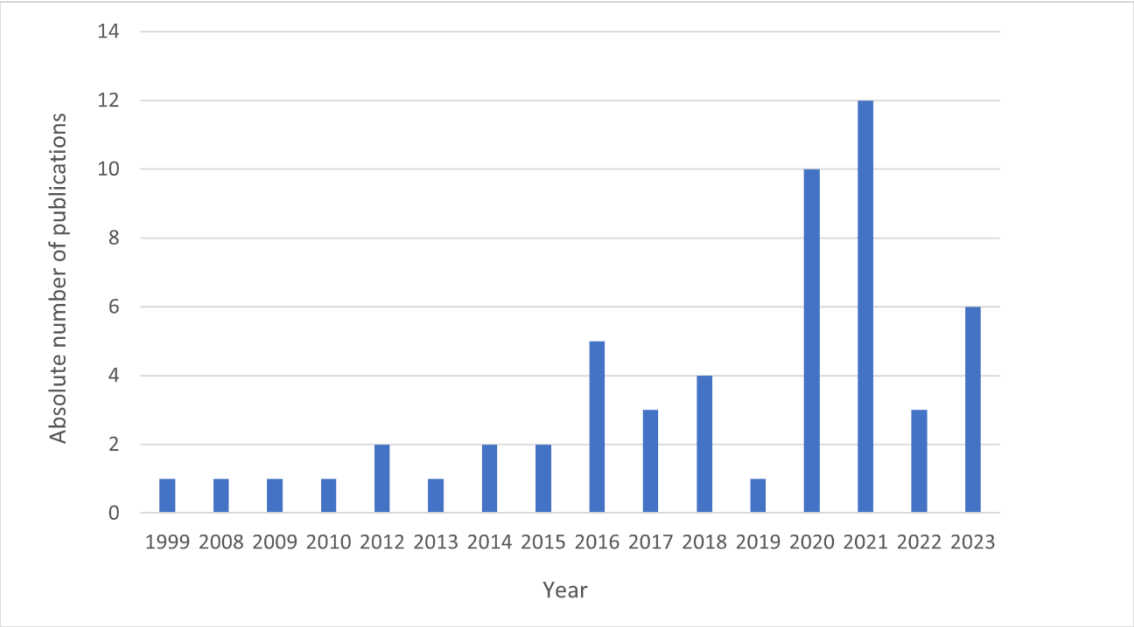

Figure 2.2 – Number of publications per year

3.1. Types of medical devices assessed by user involvement.

In our comprehensive review, we have identified a broad spectrum of medical devices (as illustrated in Figure 2.3) that have been conceived and rigorously assessed by involving end-users. The majority of the devices were seizure detection devices (44%) and healthcare / clinical information systems (40%) such as Software as Medical Device, web-based tools, electronic health records, and videoconferencing systems. VNS systems represented 9% of the studies found, followed by EEG (5%) and 1 study on an automated injection system (2%).

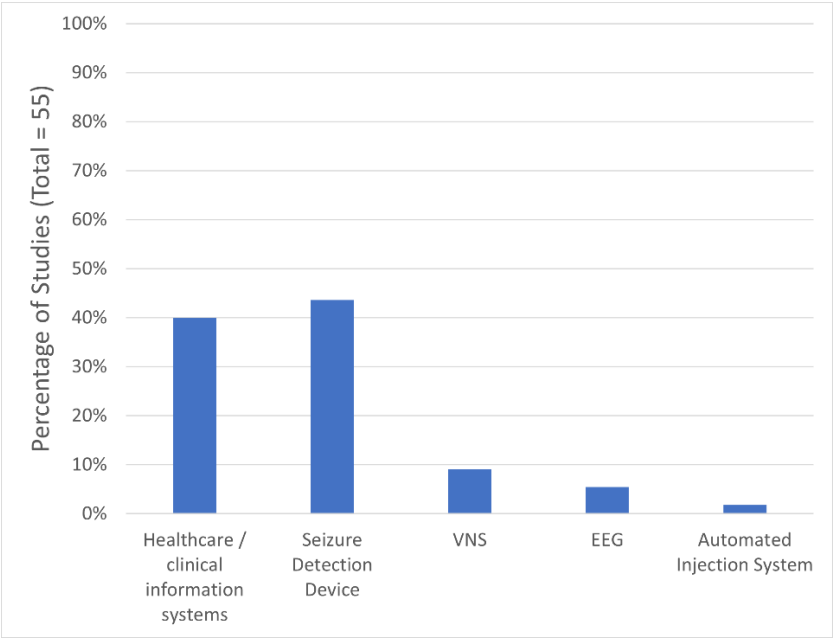

Figure 2.3 – Types of medical devices developed and assessed by user involvement (N=55)

3.2. Types of medical devices users involved in MDD and assessment.

A wide range of users were involved in the MDD process, including clinicians, PWE, carers, family members and persons with different disabilities and impairments (Figure 2.4). PWE were the users more frequently involved (40%, N = 3), followed by the PWE alongside CG (27%, N = 15) and HP (11%, N = 6). CG and HP alone were the users less frequently involved.

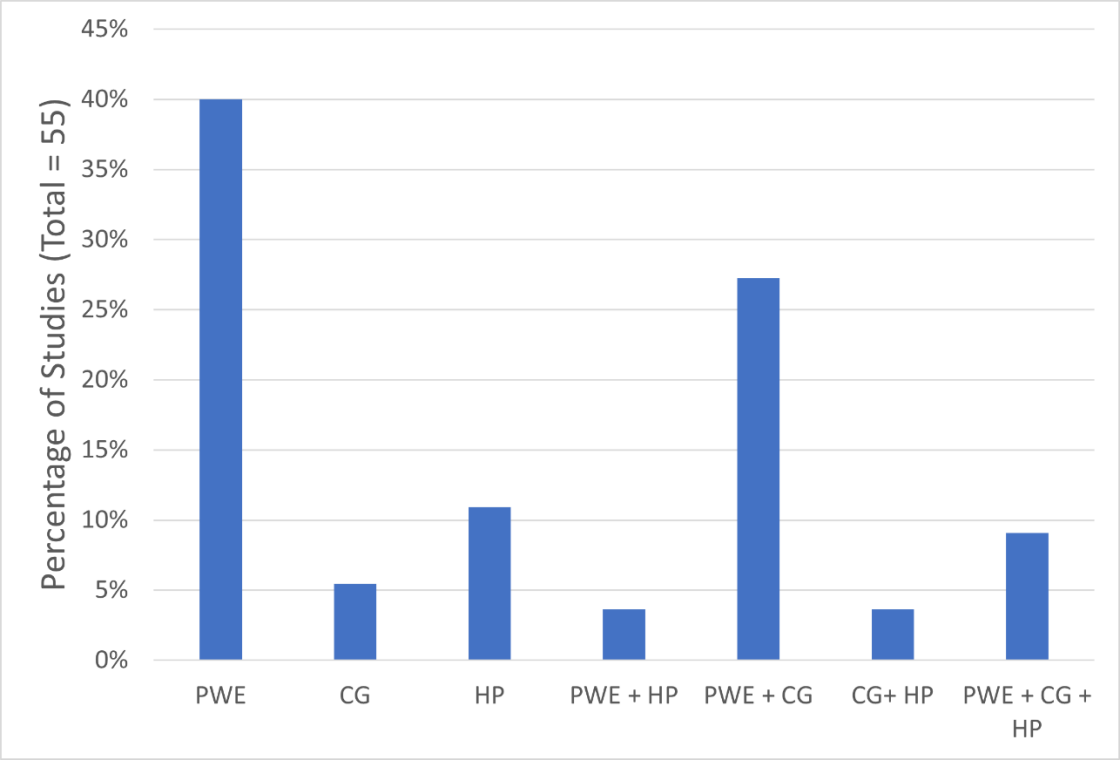

Figure 2.4 – Included publications by types of users (N=55)

3.3. Extent of user involvement by stage of the medical device lifecycle

The findings of the selected studies, especially the stages of the development of new medical devices, and methods used for capturing user perspectives by stages of the medical device lifecycle, are summarized in Figure 2.5 and Table S2. In 93% (N= 51) of the studies, users were involved in one stage of the medical device lifecycle especially in the deployment stage, and in the remaining studies users were involved in 2 (5%, N = 3) or 3 (2%, N = 1) stages of the lifecycle. Single-stage involvement was predominant in the deployment phase during which the product is already in the market, as reported in 45% (N = 25) of the studies, followed by concept stages in 25% (N = 14), when all uncertainties such as the clinical need definition, customer requirements and needs, finances, reimbursement strategy, team selection, or legal aspects must be considered. Two-stage combinations were

between design and testing and trials in 5% (N = 3). Three-stage combinations for user involvement were between concept, design, and testing and trials stages in 2% (N = 1), which is shown in Figure 2.5.

All other studies are less comprehensive as their models only encompass one stage.

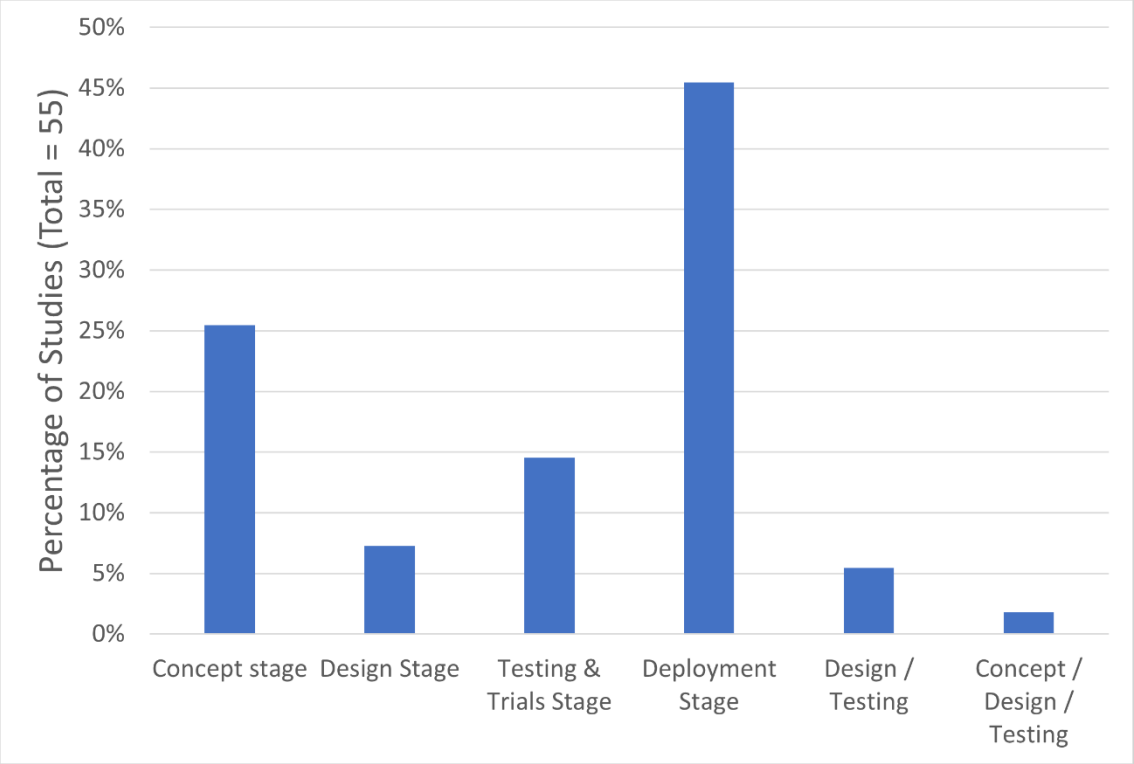

Figure 2.5 – Included publications by products lifecycle stages (N=55)

3.4. Methods used for capturing users' perspectives

Our review shows that several methods were designed to involve users, often requiring the combination of both qualitative methods to evaluate parameters from a numerical point of view and quantitative methods to indicate the user's choices, thoughts, and feelings. Involving users and capturing their perspectives in the medical device technology lifecycle concerned mostly surveys in 49% (N=43), usability testing in 20% (N=18), interviews in 19% (N=17), and focus groups in 11% (N=10) of the studies (Figure 2.6).

These methods are mapped against the medical device lifecycle stages where they were used (Table 2.2). Some of the studies used more than one method of inquiry.

Surveys and focus groups were used in all four medical device lifecycle stages where the users were involved. Typically, surveyed individuals were asked to respond to the questions in a yes/no manner, on a Likert-type scale (e.g., very often to not at all often), or with open-ended responses. The choice of responses was dictated by the investigator and the medical device (if one was used). The selection of the type of response desired was often made based on the difficulty of the question asked and the depth of knowledge and level of precision the investigator would like to have about a particular factor [17].

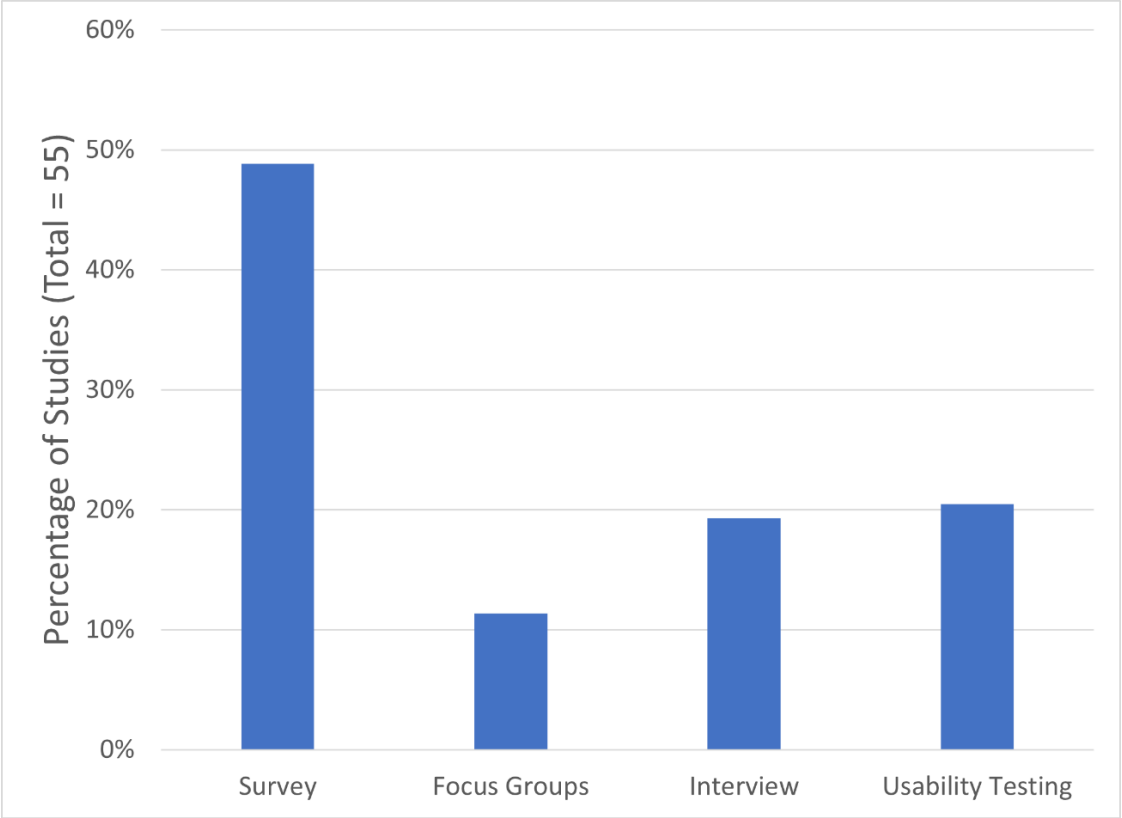

Figure 2.6 – Methods used for capturing user perspectives (N=55)

Usability tests and interviews were most commonly used for involving users and capturing their perspectives across three stages of the medical device lifecycle. During usability tests, various data collection methods were used to collect both qualitative and quantitative data.

Table 2.2 – Methods used for capturing user perspectives by stages of the medical device lifecycle (N=55)

Concept Stage	Design Stage	Test and trials stages	Deployment stage
Survey (11) Focus Groups (2) Interview (3) Usability Testing (1)	Focus Groups (4) Interviews (3) Survey (4) Usability Testing (4)	Usability Testing (6) Survey (8) Focus Groups (3)	Interviews (10) Survey (16) Usability Testing (6) Focus Groups (3)

N – total publications included

Results such as time to complete tasks, or errors made during tasks, were easy to understand and compare. In its simplest form, a usability test just involved users performing a number of typical tasks and then reporting their experiences of using the device, i.e., what, in their opinion, worked well and what was problematic in the device placement [18]. When testing an existing or prototype device to identify areas for improvement for example, qualitative data was more useful [19]. In some of the reviewed studies, the developers observed users performing scenario-based usability tests to identify shortcomings or areas for improvement [20] and/or asked the user to report their experiences in follow-up interviews [21] or through user-centered methods such as empathy interviews, empathy mapping, and persona development as they complete the task [22]. Sometimes quantitative data were collected during usability tests, such as the time taken to complete a task using the device or the number of errors made whilst performing the task [23]. Interviews were mainly semi-structured and face-to-face. The factors on which information was routinely collected in these studies include socio-demographic characteristics, lifestyle practices, medical history, and use of medical devices.

Finally, our systematic review revealed that almost half of the papers we retrieved incorporated 2 or more methods to evaluate user perspectives throughout the MDD process. For example, a scoping method such as exploratory interviews [24] or a focus group [25] were used to specify the needs and requirements of the users with an evaluative method such as a usability test [24] or survey [25] then used respectively at a later stage to determine whether these have been met.

4. Discussion

Successful medical device innovation requires research beyond technology-centred or technocentric design approaches to embrace user-centred methods [9]. Employing formal methods to involve users in the MDD process should increase the probability that devices meet proper clinical goals, comply with technical standards, are cost-effective and meet ethical norms [26].

4.1. Types of devices

In this review a substantial proportion of the devices pertained to seizure detection, and healthcare and clinical information systems. This distribution aligns with previous studies [27, 28] that highlight the predominant focus on seizure forecasting and detection in epilepsy research, underscoring the profound impact of seizures' unpredictability in this condition. Notably, only 5 VNS and 3 EEG based systems were found in our literature search. Moreover, among the 23 commercially available seizure detection devices and tools in the United States and Europe, reported by Shum and Friedman (29), only Nightwatch, Epicare, Epilog, Sensor Dots and GeneActiv were identified to have involved users in the

MDD process predominantly in the deployment phase [30-33]. This indicates a notable discrepancy in the extent of user involvement in the development of commercially available devices for epilepsy management. As highlighted by Hagedorn, Krishnamurty and Grosse (34), the disclosure of user involvement might be limited due to safety, privacy, and other ethical concerns that are unique to medical environments and contexts. Nevertheless, these results highlight a potential area for further research and improvement.

4.2. Types of users

The development of better products requires an in-depth understanding of all types of users, their activities, and their needs [35]. In epilepsy, prior research has demonstrated that distinctions among users, including PWE, CG or HP can influence the delineation of user-specific requirements [36]. Consequently, similar factors were appropriately considered in this study. Our review reveals that various types of medical devices are developed and assessed by PWE, CG and HP. These different groups of healthcare technology users' characteristics, skills and working environment may be different, which is worth considering when developing health care technologies from the users' perspective. It must be mentioned, however, that in assessing user needs, there is a substantial bias towards considering the needs of HP in contrast to PWE and CG. It is vital, therefore, that a range of users are consulted to get as wide an array of input as possible [37]. Our review showed that PWE and CG are the users more involved in the MDD process. These users are likely to be a non-medical, heterogeneous group, including family members. As a result, their background, age, level of training, physical and mental fitness, and language knowledge vary considerably. Furthermore, the context of use is hard to predict and likely to be less controlled, when compared to a healthcare setting where standardised procedures and protocols are usually in effect. Therefore, understanding their individual needs is imperative for a successful device development process, and product quality and safety [13, 15], which might be the reason why these are more involved.

4.3. Methods of involvement

In the process of designing and developing medical devices, biomedical innovators have at their disposal a range of formal methods to incorporate user requirements. Our review shows that four methods were used to involve users in the MDD process, despite several other available approaches could have been considered such as heuristic evaluation, journey mapping [38], and cognitive walkthrough [39]. The majority of the studies used surveys, probably due to their effectiveness in gathering user feedback, namely through scalability, cost-effectiveness, standardization of data, anonymity, and quick data collection [40]. With increasing attention being paid to patient-reported outcomes by funding agencies, measures

of patient-centred factors, such as quality of life, depression, anxiety, cognitive, and functional status, are increasingly included in these surveys. Usability evaluation was the second most used method, reported in 20% of the reviewed studies, probably due to the current focus on improving usability and reducing human error within the medical device industry, and their need for regulatory agencies' certification [41].

Depending on the purpose and context of the medical device, understanding user needs and eliciting their perspectives for developing medical devices could entail a combination of different methods [13]. Our systematic review revealed that nearly half of the papers we retrieved incorporated two or more methods to evaluate user perspectives throughout the MDD process. The identified use of multiple qualitative and quantitative methods in combination with specific design methods is in line with the most recent literature which highlights the importance of multi-method human-centred design approaches for the development of health innovations comprising several design cycles [42].

4.4. Stages of MDD

Human-centred design should be central to all MDD to ensure that user needs are met. It is recommended that user-centred design should begin early, and continue throughout device development [43]. Although we have found that users were involved in four out of the five stages of the MDD process - concept, design, testing and trials, and deployment stages - none of the medical devices identified was assessed in all of these four stages. Moreover the predominance of studies found in the deployment phase suggests that devices may lack sufficient user input during their development, since the form and function has already been determined, and the ability to innovate based on user needs is limited due to a number of fixed parameters [3]. Consequently, the medical devices found in this review may only partially meet user requirements or fail to meet user requirements which could result in suboptimal user experiences, higher modification costs, and missed opportunities for innovation.

4.5. Regulatory view

Despite the fact that regulatory authorities such as Food and Drug Administration (FDA) and European Medicines Agency (EMA) and international standards organizations have increasingly emphasized the importance of the employing formal methods for users' involvement in the MDD as a critical factor in ensuring the effectiveness, safety, and usability of medical devices [44]· [45], the involvement of users in the MDD process in epilepsy remains marginal. Our systematic review revealed that users were only involved in the MDD process of 13 commercially available medical devices for epilepsy management with most of the involvement being performed at the end of the MDD process in the

deployment phase. These results are in line with other therapeutic areas, as medical device manufacturers often do not consider the benefit of employing formal human factors engineering methods within the MDD process [7]. This gap suggests that the appropriate employment of formal methods by manufacturers is unlikely to occur to significant levels without deliberate efforts to encourage and support manufacturers in doing so. Alternatively, the implementation of such methods could assume a mandatory character, being dictated to manufacturers by standards and purchasing agencies.

5. Limitations

This systematic review adopted the MDD cycle comprising 5 phases accordingly with Shah and Robinson (15). However, there is a lack of standardization of the MDD life cycle phases. WHO has yet to publish the medical device innovation part of the WHO medical device technical series, where it is expected to contribute to the standardization of the stages of the MDD process. Moreover, one limitation of this systematic review lies in the potential exclusion of medical devices developed by HP, whose contributions, though integral to the development phase, may not be explicitly reported in dedicated studies. Moreover, our review is contingent on published studies, and thus, it might not capture unpublished research, proprietary assessments by companies, or start-up initiatives aimed at gathering end-users' feedback. This limitation highlights the potential underrepresentation of critical insights and developments in the field. The underreporting of user involvement in the MDD process, especially in epilepsy management, results in a missed opportunity for the broader medical community. Theoretically, once IP rights are secured, companies could safely disclose their methods of user involvement without jeopardizing their competitive position. However, the prevalent medical device industry practice of non-disclosure prevents the sharing of potentially beneficial experiences. Such transparency could foster an environment of collaborative improvement, motivating others to adopt user-centric approaches in device development. The lack of published information on user involvement methods in peer-reviewed journals hinders the opportunity for cross-learning and iterative enhancements in medical device design. This gap in knowledge dissemination ultimately impacts the quality and efficacy of devices developed for epilepsy care, as well as other medical fields. Additionally, our review found only 55 papers on user involvement or acceptability, likely because these metrics are often embedded within the paper rather than highlighted in the abstract or title. This may have inadvertently excluded relevant studies, suggesting there could be more instances of user involvement not captured in our review.

6. Conclusion and Future Direction

This systematic review elucidates the potential advantages and constraints of user involvement in MDD for epilepsy management. The analysis of 55 scientific sources reveals key findings: PWE are the most involved users, emphasizing the critical role of end-user feedback. Surveys and usability testing are common methods for gathering user input due to their scalability and cost-effectiveness. The selection of formal methods varies by device type, indicating a need for diverse qualitative and quantitative approaches. Despite user involvement in four out of five MDD stages—concept, design, testing, and deployment—there is insufficient engagement across all stages, potentially affecting device efficacy and usability. Existing regulatory guidelines stress the importance of user involvement, but more detailed guidelines are necessary for widespread adoption.

Future research should develop comprehensive guidelines that detail best practices for user involvement, ensuring early and continuous engagement. It should also broaden the scope to include caregivers and healthcare professionals, recognizing their distinct needs. Innovative methods like heuristic evaluation and journey mapping should be explored to enhance user feedback. Addressing underreporting and non-disclosure of user involvement methods is crucial, advocating for greater transparency and sharing of best practices. Additionally, research should investigate the impact of user involvement on clinical outcomes, safety, and satisfaction, providing robust evidence for user-centered design. This comprehensive approach aims to improve patient outcomes, foster innovation, and enhance efficiency in medical device development for epilepsy cared

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3.

Towards user-centered design of medical devices for SUDEP prediction and prevention: Insights from persons with epilepsy and caregivers

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Keywords

Epilepsy, sudden death in epilepsy (SUDEP), user-centered design, medical devices, seizure detection devices

Abstract

Objectives: As epilepsy management medical devices emerge as potential technological solutions for prediction and prevention of sudden death in epilepsy (SUDEP), there is a gap in understanding the features and priorities that should be included in the design of these devices. This study aims to bridge the gap between current technology and emerging needs by leveraging insights from persons with epilepsy' (PWE) and caregivers' (CG) on current epilepsy management devices and understanding how SUDEP awareness influences preferences and design considerations for potential future solutions.

Methods: Two cross-sectional surveys were designed to survey PWE and CG on medical device design features, SUDEP awareness, and participation in medical device research. Data analysis included both qualitative thematic analysis and quantitative statistical analysis.

Results: The survey revealed that among 284 responses, CG were more aware of SUDEP than PWE. Comfort was identified as the primary concern regarding wearable medical devices for epilepsy management with significant differences between PWE and CG regarding acceptance and continuous use preferences. The thematic analysis identified integration with daily life, aesthetic and emotional resonance, adaptability to seizure characteristics, and user-centric design specifications as crucial factors to be considered for enhanced medical device adoption. The integration of a companion app is seen as an important tool to enhance communication and data sharing.

Discussion: This study reveals that while SUDEP awareness can promote the development of future SUDEP predictive and preventive medical devices, these should be designed to mitigate its impact on daily life and anxiety of both PWE and CG. Comfort and acceptance are seen as key priorities to support continuous use, seen as a technical requirement of future medical devices for SUDEP prediction and prevention. Widespread adoption requires these technologies to be customizable to adapt to different lifestyles and social situations. A holistic approach should be used in the design of future medical devices to capture several dimensions of PWE and CG epilepsy management journey and uphold communication between healthcare professionals (HPs), PWE and CG.

Conclusion: Data from this study highlight the importance of considering user preferences and experiences in the design of epilepsy management medical devices with potential applicability for SUDEP prediction and prevention. By employing user-centered design methods this research provides valuable insights to inform the development of future SUDEP prediction and prevention devices.

1. Introduction

Epilepsy is one of the most common neurological chronic disorders characterized by the presence of unprovoked and recurrent seizures [1]. Despite the development of new antiepileptic drugs, between 20%–30% of people with epilepsy remain refractory to treatment [2]. Sudden Unexpected Death in Epilepsy (SUDEP) is the leading cause of epilepsy-related mortality in children and adults living with epilepsy, accounting for 1-9 patient deaths per 1000 individuals annually [3]. In the absence of novel and more efficacious antiepileptic drugs, there is a need for innovative strategies to improve epilepsy management and predict and prevent SUDEP [4]. Reliable medical devices for seizure detection have the potential to promptly alert caregivers (CG) to ongoing seizures, provide HPs with consistent data regarding seizure frequency and duration, and empower PWE by granting them greater control over their condition. Ultimately, early seizure detection could enable PWE to seek assistance, thereby mitigating the risk of SUDEP [5].

The International League Against Epilepsy and the International Federation of Clinical Neurophysiology have recently published a collaborative clinical practice guideline addressing the utilization of wearable devices for automated seizure detection [6, 7]. The expert working group identified robust evidence supporting the precise detection of generalized tonic–clonic seizures, encompassing focal-to-bilateral tonic–clonic seizures, through wearable devices. Consequently, they issued a conditional recommendation for using automated seizure detection for safety-related purposes. The clinical practice guideline underscored the need for real-world, in-field studies concerning the usability of wearable devices in the home environment for PWE and their CG' purposes. However, most studies involving PWE, and their CG focused on potential future use among individuals lacking direct experience with these devices [8-11]. The few previously published studies on direct experience with wearable devices took place within epilepsy monitoring units [12, 13] for short periods of time (days), with only a limited number exploring usability and outcomes in the home environment and examined a single device type, overlooking broader experiences [14-16]. This highlights the necessity for further research and development in this area, with a specific focus on designing devices that effectively address the unique needs and challenges faced by PWE and their CGs.

User-centered design is increasingly being recognized and adopted in the medical device industry as a means to enhance medical device effectiveness, usability, and user satisfaction. Using this approach, users such as PWE, CG, and HPs can be seen as sources of innovation. Manufacturers can identify unique insights by asking about their needs or, even more effectively, observing them during the use of existing medical devices and tracking their behaviour in real-world studies. This ensures that the final medical devices meet users specific needs and preferences [6, 7], [17]. Despite its recognized importance, there is a notable gap in the literature concerning user-centered research in the design of epilepsy management medical devices. Ferreira et al. [18] found only 55 scientific sources pertaining to user engagement in medical device design and development for epilepsy between 1999 and 2023, capturing their perspectives mainly through surveys. Although PWE and CG were the primary participants in user involvement, only two studies [4, 11] have compared the results obtained from these two populations. Moreover, users played a role in the development process of only two commercially available medical devices for epilepsy management [18]. This gap underscores the importance of user-centered design methods in the design of medical devices specifically for epilepsy management, particularly in the context of SUDEP prediction and prevention. Medical device design features [3], SUDEP awareness [19], and participation in medical device research [20] are all crucial aspects mentioned in the development medical devices for epilepsy management. Together, these components contribute to the development of medical devices that are both clinically robust and address the unique needs and challenges faced by PWE and CG. For epilepsy, where management is not just about controlling seizures but also about improving quality of life, user-centered design offers a pathway to develop more effective and empathetic solutions. Therefore, this study aims to gather specific design preferences for medical devices, contributing to generating a comprehensive list of user requirements that will guide the design process of a tailored medical device prototype for SUDEP prevention, marking a significant step forward in user-centered design for epilepsy management. Furthermore, it also aims to delve into the experiences and perceptions of PWE and their CG regarding SUDEP, as well as their attitudes towards using medical devices and the factors influencing their willingness to adopt such technologyd

2. Methods

2.1. Study design and sample

The NEUROSENSE Project (www.neurosense-project.eu) aims to develop a medical device prototype that uses artificial intelligence (AI) to recognise life-threatening seizures and automatically intervene to prevent SUDEP. Recognizing the importance of user-centered design in the medical device development process, the NEUROSENSE Consortium has

initiated a structured series of design thinking workshops. This cross-sectional survey study corresponds to the first workshop and used a convenience sampling of 284 PWE and CG. Based on the gathered results, a second workshop will be conducted to assess how the key values identified in the first workshop are integrated into the preliminary design of the intended medical device prototype. Subsequently, a third workshop will be organized as a further iteration to collect feedback from end-users on a refined prototype. A systematic review of literature was undertaken to identify validated questionnaires regarding user preferences for seizure detection devices [18]. While questionnaires addressing epilepsy management devices were discovered, no validation was found. Consequently, the criterion validity of our questionnaire remains unverified. Participants were invited through social media, newsletters, mailing lists, websites, blogs, membership communications, or in clinics of partner organizations, advocacy groups, professional organizations, community agencies, and health research institutions. Moreover, paper flyers with QR-codes were mailed to epilepsy monitoring units and non-profit community epilepsy agencies if requested by staff members.

2.2. Data Collection

We used an anonymous online survey distributed via the NEUROSENSE public website (www.neurosense-project.eu) between April 1, 2023, and July 31, 2023. The use of online surveys offers advantages such as faster data collection, cost-effectiveness, real-time analysis and unrestricted geographic coverage [21]. The survey was available in eight languages to ensure inclusivity and reach a wider audience, aligning with the practice of multilingual surveys to enhance data accuracy. To validate the surveys in multiple languages, linguistic validation techniques were employed, ensuring linguistic and cultural equivalence across translations [22]. The questionnaire, developed in compliance with General Data Protection Regulation (GDPR) guidelines, underwent review by the NEUROSENSE Patient Advisory Board (PAB) to ensure ethical and patient-centric design [22]. The survey comprised sections tailored for CG and PWE, to ensure a comprehensive data collection to inform future device development and SUDEP prevention strategies. In this survey, only adults aged more than 18 years were included as participants. An initial disclaimer was provided, segmented into four parts, to communicate the objectives and framework of the NEUROSENSE project, the purpose of the survey, the voluntary nature of participation, and the methods used for data management. The survey was divided into two distinct sections, one tailored for CG and the other for PWE. The section intended for PWE comprised 11 questions, while the CG-oriented section consisted of 12 questions. Demographic questions included information about age range. Other questions included information about 3 main categories: medical device design features, SUDEP awareness

and participation in research of medical devices. The final version of the questionnaire can be seen in Supplementary Material.

2.3. Data Analysis

Qualitative data analysis

All open-ended responses underwent thematic analysis. Standardized grounded theory coding steps including a series of processes such as data collection, data analysis and theory coding was used. Standardized grounded theory coding steps [23] including a series of processes such as data collection, data analysis and theory coding was used. Three authors (JF, MF and RP) manually coded the data. The coding process was performed separately by the three authors over multiple iterations, with the authors meeting to discuss connections between the codes and agree on emerging themes at each stage. Ambiguities and discrepancies were discussed by the three raters and compared to supporting context within the dataset (i.e., descriptions of thoughts, feelings, perceptions, PWE vs CG) until agreement was reached. The everyday activities and seizure description listed by participants were first categorized using open coding, and then analyzed again with a revised scheme based on the remaining open-ended descriptions. An axial and selective coding process was then used to derive meaning with respect to developing medical device priority hierarchies.

Quantitative data analysis

Closed-ended questions were analysed with the Software Package for Social Sciences (SPSS) Version 28.0. The significance level was fixed at 0.05. Descriptive statistics included absolute (n) and relative (%) frequencies for categorical variables, and median and percentile 25 and 75 (P25 and P75, respectively) for ordinal continuous variables. The normality of the variables under study was analysed to apply the most appropriate statistical tests. Mann–Whitney U test and $\chi 2$ or Fisher's exact test, respectively for continuous and categorical variables, were used to compare the survey responses provided by PWE and by CG. Additionally, Spearman coefficients were used to study the correlations between the level of change in daily life activities due to SUDEP risk awareness and the level of anxiety regarding SUDEP risk among participants reporting SUDEP risk awareness.

2.4. Ethical considerations

This study was conducted according to the principles of the Helsinki Declaration. The study protocol was evaluated and approved by the Ethics Commission of the *Instituto de Investigação e Inovação em Saúde da Universidade do Porto* (i3S). All participants provided written informed consent.

3. Results

3.1. PWE and CG demographics

Table 3.1 shows that almost 60% of the participants were CG. It also shows that the age group more reported by all participants was the range "40 to 55 years old". Still, PWE reported being significantly younger than the CG (p=0.031).

Table 3.1 – PWE and CG demographics

	PWE	*CG*	p-value
Total, n (%)	114 (40.1)	170 (59.9)	-
Age Group, n (%)			
18 to 24 years old	10 (8.8)	17 (10.0)	
25 to 34 years old	33 (28.9)	23 (13.5)	
35 to 39 years old	16 (14.0)	26 (15.3)	
40 to 55 years old	46 (40.4)	84 (49.4)	
More than 56 years old	9 (7.9)	20 (11.8)	**0.031***

* χ 2 test.

3.2. Medical Device Design

3.2.1. Direct Questions

3.2.1.1. Device features

Overall, comfort was the most commonly reported concern regarding wearable medical devices for epilepsy management (Table 3.2). CG showed significantly greater concern about acceptance (28.2% vs 9.8% in PWE), whereas PWE reported not having any concerns more often (21.1% vs 10.6% in CG). Moreover, the majority favoured devices detecting all proposed events, with significant preference among CG (75.3% vs 59.6% in PWE, p=0.010). Continuous monitoring was highly preferred, but no statistically significant difference was found between groups (p=0.072). PWE showed significant higher willingness for continuous 24/7 device usage compared to CG (65.8% vs 46.5%, p=0.005).

3.2.1.2. Healthcare mobile application feature importance

Both PWE and CGs showed interest in receiving notifications through an epilepsy-related healthcare mobile application (Table 3.2). Notably, there was a significant higher interest for social messages or social networks among PWE (36.0% vs 18.2% in CG, p=0.001), and a significant higher interest on changes in health status notifications among CG (86.5% vs 74.6%, p=0.017).

3.2.1.3. Healthcare Mobile Application Setup and Data Sharing

Preferences for the time commitment required to customize the mobile application significantly differed between the groups ($p<0.001$), with CGs showing a greater willingness to spend time on customization (Table 3.2.). While some preferred medical staff to manage the setup entirely, others favoured a joint effort with medical staff or independent setup with instructions and support. Overall, both PWE and CGs exhibited a high level of trust in sharing medical data with HPs via the mobile application.

Table 3.2 – Desired design features

	PWE	*CG*	p-value
The biggest concern regarding the use of a wearable medical for epilepsy monitoring/management, n (%)			
Acceptance	11 (9.6)	48 (28.2)	
Portability	14 (12.3)	15 (8.8)	
Comfort	35 (30.7)	46 (27.1)	
Absence of adversity	17 (14.9)	18 (10.6)	
Daily management	9 (7.9)	13 (7.6)	
I have no concern	24 (21.1)	18 (10.6)	
Other	4 (3.5)	12 (7.1)	**0.003***
Events to be detected with an alarm by a wearable medical device for epilepsy monitoring/management, n (%)			
Seizures	35 (30.7)	37 (21.8)	
Absences	5 (4.4)	2 (1.2)	
Irregular heartbeats or irregular breathing	5 (4.4)	1 (0.6)	
All of the above	68 (59.6)	128 (75.3)	
Other	1 (0.9)	2 (1.2)	**0.010****
Moment to detect those events, n (%)			
Always	101 (88.6)	147 (86.5)	
Only in wakefulness	7 (6.1)	4 (2.4)	
Only during sleep	6 (5.3)	19 (11.2)	0.072*
Willingness to use a wearable medical device 24/7 for epilepsy monitoring/management, n (%)			
Yes	75 (65.8)	79 (46.5)	
Maybe	34 (29.8)	75 (44.1)	
No	5 (4.4)	16 (9.4)	**0.005***
Level of comfort in sharing medical information through an epilepsy-related healthcare mobile application, median (P25, P75)			
With doctor [a]	1 (1, 2)	1 (1, 2)	0.300***

With caregiver [a]	1 (1, 2)	-	-
Person to set up an epilepsy-related healthcare mobile application, n (%)			
100% medical staff	30 (26.3)	27 (15.9)	
50% medical staff + 50% myself	51 (44.7)	88 (51.8)	
100% myself	5 (4.4)	13 (7.6)	
100% myself with instructions from manufacturer and a help desk	27 (23.7)	38 (22.4)	
Other	1 (0.9)	4 (2.4)	0.180**
Time to customize an epilepsy-related healthcare mobile application, n (%)			
Less than 5 minutes	28 (24.6)	13 (7.6)	
5 to 10 minutes	39 (34.2)	45 (26.5)	
10 to 20 minutes	38 (33.3)	87 (51.2)	
Other	9 (7.9)	25 (14.7)	**<0.001***
Notifications regarding "Changes in health status" in an epilepsy-related healthcare mobile application, n (%)			
Yes	85 (74.6)	147 (86.5)	**0.017***
Notifications regarding "Latest news about SUDEP" in an epilepsy-related healthcare mobile application, n (%)			
Yes	48 (42.1)	83 (48.8)	0.321*
Notifications regarding "Medical appointments, medication reminders or medication tracker" in an epilepsy-related healthcare mobile application, n (%)			
Yes	82 (71.9)	128 (75.3)	0.620*
Notifications regarding "Social messages or social networks" in an epilepsy-related healthcare mobile application, n (%)			
Yes	41 (36.0)	31 (18.2)	**0.001***
No notifications in an epilepsy-related healthcare mobile application, n (%)			
Yes	11 (9.6)	2 (1.2)	**0.002***

PWE, persons with epilepsy; CG, caregivers.

* χ 2 test; **Fisher's exact test; *** Mann–Whitney U test.

[a] Range from 1 (very comfortable) to 5 (very uncomfortable).

3.2.2. Indirect Questions

From the open questions, four key themes in designing epilepsy medical devices were identified: integration with daily life, aesthetic and emotional resonance, adaptability to seizure characteristics and user-centric design specifications (Table 3.3). This

identification emphasizes the need for devices to accommodate diverse lifestyle patterns, including both active and sedentary activities, while remaining socially inconspicuous. In the category of aesthetic and emotional resonance, themes like comforting, personal, and natural underscore the importance of emotional engagement and a design that blends with the user's environment. Adaptability to seizure characteristics highlights the need for customizable features to support recovery and cater to individual seizure patterns. User-centric design specifications emphasize the critical role of physical design elements, such as size, colour, and shape, in enhancing user acceptance and comfort. The findings advocate for a holistic design approach that prioritizes user comfort, aesthetic appeal, and individual preferences to ensure long-term satisfaction and adherence.

Table 3.3 – Factors perceived as important to be considered in the design of epilepsy management devices by PWE and CG.

Selective Coding	Axial Coding (Opening Coding Numbers)	Sub-Total for Opening Codes
Integration with Daily Life The device must be adaptable to various activities (Active, Indoor, Outdoor). It should blend into the user's lifestyle seamlessly, ensuring comfort during both active and sedentary activities.	Active (51), Indoor (72), Outdoor (26), Social (9), Solitary (0)	158
Aesthetic and Emotional Resonance Design elements that evoke comfort, personalization, and a natural feel (Comforting, Personal, Natural) are crucial. The device should not only be functional but also emotionally resonant, providing a sense of calm and familiarity.	Comforting (45), Personal (31), Natural (31), Familiar (0)	107
Adaptability to Seizure Characteristics The device should cater to the specific needs arising from different seizure patterns (Frequency, Duration, Post-Seizure). Features that assist during and after a seizure are vital, such as easy-to-use controls during an episode and post-seizure care functions.	Frequency (13), Duration (11), Post-Seizure (48), Intensity (0), Warning Signs (0)	72
User-Centric Design Specifications Size, color, and shape considerations (Size, Color, Shape) are important for user comfort and acceptance. The device should be customizable to cater to individual preferences and physical requirements.	Size (42), Color (16), Shape (11), Texture (0)	69

3.3. SUDEP Awareness & willingness to participate in research

CG exhibit significantly higher awareness of SUDEP compared to PWE (86.5% vs 58.8%, p<0.001) (Table 3.4). Additionally, among those who reported SUDEP risk awareness, CG experience a significant greater impact on daily life activities and significant higher anxiety levels due to SUDEP awareness compared to PWE. The level of change in daily life activities positively correlates with anxiety regarding SUDEP risk, both among PWE and CGs (respectively, ρ =0.493 and p<0.001; and ρ =0.481 and p<0.001). Moreover, the readiness to participate in a study to test a medical device was high among both PWE and CG (Table 3.4).

Table 3.4 – SUDEP Risk Awareness, Impact on Daily Life, Anxiety Levels, and Willingness to Participate in Medical Device Study among Patients with Epilepsy and Caregivers

	PWE	*CG*	p-value
SUDEP risk awareness, n (%)			
Yes	67 (58.8)	147 (86.5)	**<0.001***
For participants with SUDEP risk awareness, median (P25, P75)			
Level of change in daily life activities due to SUDEP risk awareness [a]	5 (2, 7)	9 (7, 10)	**<0.001****
Level of anxiety regarding SUDEP risk [a]	5 (3, 8)	9 (7, 10)	**<0.001****
Willingness to participate in a study to test a wearable medical device for epilepsy monitoring/management, n (%)			
Yes	78 (68.4)	124 (72.9)	
Maybe	32 (28.1)	40 (23.5)	
No	4 (3.5)	6 (3.5)	0.687*

[a] Range from 1 (not at all) to 10 (very much).

* χ 2 test; ** Mann–Whitney U test.

PWE, persons with epilepsy; CG, caregivers; SUDEP, Sudden Unexpected Death in Epilepsy.

4. Discussion

This study aimed to provide user-centered information for designers of future SUDEP prediction and prevention devices, regardless of current technological limitations. Through a combination of open-ended and closed-ended questions spanning three primary domains – medical device design features, SUDEP awareness, and participation in medical device

research – PWE and CG desired features were identified for future SUDEP prediction and prevention devices. These findings can inform device design.

The survey disclosed a significantly higher **SUDEP awareness** among CG (86.5% vs. 58.8% in PWE). This is in line with Kroner, Wright (24) and suggests a potential gap in communication between HPs and PWE as many HPs are hesitant to discuss SUDEP because of the perception of evoking unnecessary fear in patients [25]. The limited awareness of SUDEP among PWEs can have critical implications in the design and efficacy of future medical devices aimed specifically at SUDEP prevention. This knowledge gap can lead to an underappreciation of the necessary features in such devices, both by PWE, CG and HPs which might lead to the creation of devices that do not adequately address the specific needs associated with SUDEP. An integral part of the medical device design development process is the conduction of clinical studies for usability and performance testing. In our study, CGs who were more aware of SUDEP showed a significantly higher willingness to participate in such studies ($p<0.001$). This contrasts with the PWE group, where no significant correlation was found ($p=0.282$). These findings, aligned with the recent literature [26], highlight the potential for leveraging SUDEP awareness to enhance participation in research and development initiatives, a strategy that could be beneficial in designing and testing new SUDEP prediction and prevention technologies. Furthermore, an increased understanding of SUDEP among PWEs is critical for the effective deployment and utilization of the current seizure monitoring and alerting technologies. These devices, although not designed for SUDEP prediction and prevention, play a vital role in early seizure detection and intervention which could significantly reduce SUDEP risk.

The impact of SUDEP awareness on daily life activities and anxiety is also reflected in our results, being more pronounced among CG in agreement with the studies by [25], which noted experienced anxiety in CG after SUDEP disclosure. This heightened concern among CG reflects their deeper emotional involvement and sense of responsibility, underscoring the emotional toll on CG. The dynamics where CG may be more emotionally involved and aware of their responsibilities towards PWE resonates with findings from Zhang, Zhang (27) and Yang, Ji (28). Their results demonstrate that anxiety and depression status are common in CGs, namely in the form of guilt, stigma, anxiety, nervousness, and loss of control. The design of future SUDEP predictive and preventive medical devices should therefore mitigate the impact of SUDEP awareness on daily life and anxiety. The independence of SUDEP awareness and willingness to wear devices, as indicated by the p-values for both PWE and CG groups, suggests that the decision to use a wearable device is influenced by factors other than just awareness of SUDEP risks, a perspective that broadens the scope of considerations in device adoption and usage.

Within this set of factors, comfort rated highest among respondents concerns regarding epilepsy management medical devices. The priority given to device comfort by

both PWE and CG parallels observations in healthcare technology adoption studies [29], emphasizing the necessity for device designs that seamlessly blend into the everyday routines of PWE and their CG. This is reinforced by the prominence of 'Activity-Device Interaction' in our findings. The diversity of activities, both active and sedentary, suggests that the device should be versatile enough to accommodate a wide range of physical movements and environments. This finding aligns with previous research emphasizing the importance of device adaptability in chronic disease management [30]. Particularly, the absence of 'Solitary' activities might indicate a social context in the lives of these individuals, further hinting at the need for a device that is discreet yet functional in social settings. This insight challenges designers to create solutions that are not only medically effective but also socially and emotionally considerate. Responses indicating preferences for 'Comforting', 'Personal', and 'Natural' elements in objects of daily use also point towards a significant emotional dimension in device design. This aligns with recent trends in human-centered design, which emphasize emotional resonance and personalization in medical devices [31]. The emotional bond between the user and the device can play a critical role in long-term engagement and adherence to treatment regimes. Furthermore, the absence of 'Familiar' objects in responses might suggest an opportunity for innovation in device design, where new forms of familiarity and comfort can be explored and integrated. The qualitative analysis also highlights the importance of 'Device Condition Requirements', with a significant focus on size, color, and shape. This is in line with user-centered design principles, suggesting that the physical attributes of a device significantly impact user acceptance and comfort [32]. The emphasis on 'Size' indicates a preference for compact and non-intrusive devices, which is crucial for continuous wearability and discretion. The varied preferences for 'Color' and 'Shape' suggest a demand for personalization, resonating with the broader trend towards individualized healthcare solutions.

The concern for device acceptance, particularly among CGs, highlights the importance of social acceptance in wearable technology, indicating that such designs should promote a continuous use, recognized by CGs as a critical element for effective epilepsy monitoring and management [33]. In line with the literature, most of the participants expressed their willingness to continuously use wearable medical devices. This result aligns with the perceived need to detect different events both during wakefulness and during sleep. This acceptance is crucial as it establishes a technical prerequisite for any SUDEP predictive and preventive medical device. SUDEP, being unpredictable and potentially occurring anywhere at any time, necessitates constant monitoring. Hence, the demonstrated readiness of participants to constantly wear such devices reflects positively on their feasibility and potential effectiveness in mitigating SUDEP risks. Incorporating continuous monitoring features in wearable medical devices aligns with the imperative need for timely detection and intervention in SUDEP cases.

The qualitative analysis also revealed a clear need for devices tailored to the specific seizure characteristics of individuals. The high mention of 'Post-Seizure' aspects suggests that features aiding recovery and comfort after seizures are crucial. This novel finding is supported by literature emphasizing post-seizure care in epilepsy management [34]. The importance of post-seizure features in seizure detection device design stems from various factors. Firstly, it ensures the safety and comfort of individuals after an episode, with features such as alerts to caregivers and mechanisms to prevent injury during recovery [35]. Monitoring the post-seizure period is also crucial for understanding recovery and providing timely medical intervention if necessary. Additionally, effective post-seizure care can alleviate anxiety for PWEs and CGs, enhancing overall quality of care. Finally, addressing post-seizure needs contributes to comprehensive epilepsy management strategies beyond seizure detection alone, supporting long-term care. The data discloses a lower emphasis on 'Frequency' and 'Duration', which might indicate a variability in seizure patterns among respondents, further advocating for customizable device features.

These insights call for a holistic approach that can guide the development of devices that not only detect and manage seizures but also support the user's journey by significantly improve safety, recovery monitoring, and overall quality of life for PWEs and their CGs. An effective communication between PWEs, CGs and HPs can be pivotal to achieve this holistic approach. Survey respondents' willingness to share data with doctors and CGs is a valuable asset for developing future epilepsy management devices. This aligns with findings from Floch, Zettl (30), who reported that continuous monitoring and the ability to share seizure activity with caregivers were both considered important by the population they surveyed. The motivation of both PWEs and CGs to share data with medical staff is a crucial aspect that should be incorporated into the design of medical devices although not extensively discussed in the literature. Our findings are in agreement with the broader trend in healthcare where patient data sharing is increasingly becoming integral to personalized care [36]. This should be seen as a key strength to be explored to enhance communication between PWEs, CGs and HPs in the design and development of new devices for SUDEP.

In epilepsy, mobile health apps are opening up new lines of communication which, in turn, are improving accessibility, provide real-time monitoring, and enhancing the patient education and epilepsy management [37]. The survey results show a strong interest in receiving notifications through an epilepsy-related healthcare mobile app among PWEs and CGs. Both groups prefer notifications on health status changes, medical appointments, and medication reminders. However, there is a difference in interest regarding SUDEP news, with CGs showing slightly more interest. There is also a disparity in interest in social notifications, with PWEs being more interested than CGs. Some participants preferred not to receive any notifications. Regarding setup preferences, most PWEs and CGs prefer a joint effort with medical staff, highlighting the importance of collaboration in managing

healthcare. In summary, the survey underscores the need for customizable notifications and collaborative setup approaches in designing an epilepsy-related healthcare app to cater to the diverse preferences of PWEs and CGs.

5. Limitations

This study has some limitations that need to be considered. Firstly, due to the lack of SUDEP awareness and the absence of currently available devices for SUDEP prediction or prevention we did not directly ask about the characteristics of a device to predict and prevent SUDEP but rather inquired about the impact of SUDEP on the quality of life of PWEs and CGs. While direct applicability of these findings to a SUDEP-specific device remains uncertain, the insights gathered from these questions could potentially provide limited guidance on the potential features such a SUDEP predictive and preventive medical device may need in the future. Furthermore, the novelty of our research approach and the lack of specific information about different types of epilepsy/seizures may impact the generalizability of the findings. In addition, our survey was designed to be anonymous and collected limited personal information. It was distributed mainly through social media, which may have introduced a bias due to selective non-response. To overcome these limitations, future studies should aim to collect more personal information in a larger and more diverse population.

We also did not seek the perspectives of medical professionals and other formal CGs, which could have added valuable insights. However, it's important to note that our primary goal was to understand the basic needs of potential users of epilepsy management devices. While our survey may not provide comprehensive customer validation, it does offer valuable insights by capturing the views of PWEs and CGs, supporting the design of more user-focused devices. Additionally, the subjective nature of the responses and the lack of validation for question accuracy could introduce unintended biases. We intentionally did not focus into detailed sensor descriptions to maintain a patient-centered focus. Despite these limitations, our survey results can be a valuable resource for developers of wearable seizure detection and recognition devices, highlighting the importance of considering PWEs and CGs preferences in addressing existing gaps in healthcare product development.

6. Conclusion and Future Direction

Our study provides preliminary insights that could guide future research specifically aimed at developing future medical devices aimed at predicting and preventing SUDEP. Despite existing gaps in our understanding of SUDEP, our findings reveal a promising inclination

towards user acceptance of wearable medical devices for continuous use, a fundamental prerequisite for effective SUDEP prevention. We advocate for the adoption of user-centered design principles as a decisive approach to propel innovation in the realm of SUDEP prevention and management. We emphasize the necessity for designers to adopt a holistic approach throughout the design and development phases of new medical devices. Key considerations such as comfort and acceptance emerge as pivotal factors in enhancing usability. We propose the integration of a "companion app" as an effective strategy to address this holistic perspective.

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4.

Artificial Intelligence driven Closed-Loop Devices in SUDEP Prediction and Prevention: Insights from Persons with Epilepsy and Caregivers

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Keywords

epilepsy, sudden death in epilepsy, closed loop system, artificial intelligence, automated intervention, user involvement, medical device, wearable device, medical device design

Abstract

Objectives The absence of strategies for predicting and preventing Sudden Unexpected Death in Epilepsy (SUDEP) is intertwined with the lack of studies measuring users' attitudes towards potential innovative interventions. The current study introduces the potential use of Artificial Intelligence-driven Closed Loop Devices (AI-CLDs) in SUDEP prediction and prevention, while assessing persons with epilepsy (PWEs) and caregivers (CGs) attitudes towards AI-CLDs' potential adoption and implementation.

Methods A qualitative study was conducted through three focus groups involving PWEs and CGs. Participants were recruited through the NEUROSENSE Patient Advisory Board, with discussions facilitated through a semi-structured interview guide. The study followed grounded theory and qualitative content analysis methods to evaluate the perspectives of PWEs and CGs on the potential use of AI-CLDs in SUDEP prediction and prevention. Data was collected between October 2024 and February 2025, with all sessions transcribed and analysed.

Results Three main areas for consideration emerged from the analysis: expectations on AI-CLDs for SUDEP prediction and prevention, decision-making processes involving AI use in healthcare, and barriers and facilitators to AI-CLDs adoption. PWEs and CGs generally expressed positive attitudes toward AI-CLDs, showing support for automatic data sharing with healthcare providers and real-time alerts. However, concerns about AI system accuracy, over-reliance on automation and the need for control over interventions were raised. Both groups preferred wearable devices over implanted solutions, emphasizing comfort and discretion as critical factors for adoption.

Significance This study highlights the potential of AI-CLDs in improving the prediction and prevention of SUDEP, showing promise for enhancing patient safety through real-time monitoring and interventions. The findings underscore the importance of user-centered design in device development, emphasizing comfort, control over interventions, and integration into daily life. This research provides important insights for future development, aiming to improve PWEs and CGs confidence in using AI technologies for epilepsy care and risk management.

Plain Language Summary The present study looks at how people with epilepsy and their caregivers feel about using devices powered by Artificial Intelligence (AI) to predict and prevent Sudden Unexpected Death in Epilepsy (SUDEP). The results indicate that most of the participants have a positive opinion about these devices, particularly the wearable ones, and consider automatic alerts and sharing data with healthcare providers acceptable. However, concerns were raised about AI making decisions without enough human oversight, and the need to ensure that the technology is reliable and does not disrupt daily routines.

1. Introduction

Sudden Unexpected Death in Epilepsy (SUDEP) is the leading cause of epilepsy-related mortality, with an estimated incidence of 1.2 per 1,000 person-years in individuals with epilepsy, increasing significantly in drug-resistant epilepsy [1]. The exact mechanisms underlying SUDEP remain unclear, but autonomic dysfunction, seizure-related respiratory depression, and cardiac abnormalities have been implicated [2]. Given the unpredictability and lethality of SUDEP, there is an urgent need for novel risk assessment and prevention strategies. Existing SUDEP prevention efforts primarily focus on seizure control, nocturnal monitoring, and lifestyle modifications. However, these approaches remain insufficient in mitigating risk, as many cases occur unexpectedly, even in individuals receiving optimal medical treatment [3]. Current monitoring devices, such as wearable seizure detectors, have limitations in sensitivity and specificity, often leading to false alarms and limited real-time intervention capability [4]. Recent advances in artificial intelligence (AI) have shown promise in improving epilepsy management by enabling seizure prediction, automated detection, and personalized treatment approaches [5]. Machine learning algorithms trained on multimodal physiological data, such as electroencephalography (EEG) [6], ECG [7], and respiratory patterns [8], have demonstrated the potential to identify pre-seizure states and high-risk conditions [9]. Given these advancements, AI-based solutions could play a pivotal role in SUDEP risk stratification and intervention [10]. AI-driven closed loop devices (AI-CLD) are an emerging technology in digital health that integrates real-time data acquisition, AI-based predictive modelling, and automated interventions [11]. In these systems, the computational algorithms analyses real-time physiological data, adjusts control variables, and uses actuators to deliver energy or materials to maintain the target physiological level [12]. This integration allows AI-CLDs to be successfully applied in neurological disorders, such as Parkinson's disease and epilepsy, for optimizing deep brain stimulation and seizure control [13, 14].These emerging devices may have the potential to revolutionize the

standard of care by ensuring adequate and timely therapy delivery in an emergency setting, reducing cognitive overload, minimizing human error, and enhancing medical care during surge scenarios such as a life-threatening seizure [15]. Designed as wearable devices, AI-CLDs for SUDEP prediction and prevention should support continuous use while ensuring practicality, real-time responsiveness, and prioritizing user comfort and acceptance [16]. Despite AI-CLDs hold significant potential for SUDEP prediction and prevention, this remains an emerging field, and the concept has yet to be thoroughly explored. Moreover, the successful implementation of AI-CLDs in SUDEP prediction and prevention requires the acceptance and trust of users, including persons with epilepsy (PWEs) and their caregivers (CGs). Factors such as integration with daily life, aesthetic and emotional resonance, adaptability to seizure characteristics, and user-centric design must be taken in consideration to promote safe and effective use of these devices [16]. Additionally, the design and development process must addres ethical considerations, data privacy concerns, usability challenges, and potential psychological impacts [17]. This study aims to introduce, for the first time, the potential application of AI-CLDs as a novel approach for SUDEP prediction and prevention while exploring the perspectives of PWEs and CGs regarding the adoption and use of these technologies.

2. Methods

2.1. Description of the NEUROSENSE Project and Proposed AI-CLD

The NEUROSENSE Project (http://www.neurosense-project.eu) aims to identify novel SUDEP-predictive neuroendocrine biomarkers in interstitial fluid (ISF) and develop an AI-CLD prototype to recognise life-threatening seizures and prevent SUDEP through automatic intervention (Figure 4.1). By using ISF as a matrix for biomarker detection, the intended prototype consists in a wearable device that can be autonomously applied by the patient to the skin and remain in place for several days. The foreseen AI-CLD system (Figure 4.1) comprises four key components: (i) a continuous seizure detection sensor, (ii) a continuous sensor monitoring the SUDEP biomarker, (iii) a processor, and (iv) an actuator - emergency drug delivery system. When the device is applied to the skin (Figure 4.2 – action 1), ISF is sampled continuously through minimally invasive microneedles (Figure 4.2 – action 2) and the SUDEP biomarker is quantified in real time by the device's sensor. When a seizure occurs, the seizure detection sensor activates the AI-CLD processor (Figure 4.2 – action 3), which analyses the data generated by the biomarker sensor using a

built-in algorithm. The algorithm, trained on historical data from the recorded patient's biomarker patterns during seizures, analyses the data in real-time to assess the risk of SUDEP. When a high-risk seizure is identified (Figure 4.2 – action 4), the AI-CLD

Figure 4.1 Overview of the AI-CLD system, consisting of a continuous seizure detection sensor, a SUDEP biomarker sensor, a processor, and an emergency drug delivery actuator

processor immediately triggers the actuator to deliver a SUDEP preventing intervention, e.g., an appropriate dose of a SUDEP preventing medication (Figure 4.2 – action 5). Simultaneously, the AI-CLD communicates with a mobile device (Figure 4.2 – action 6) to

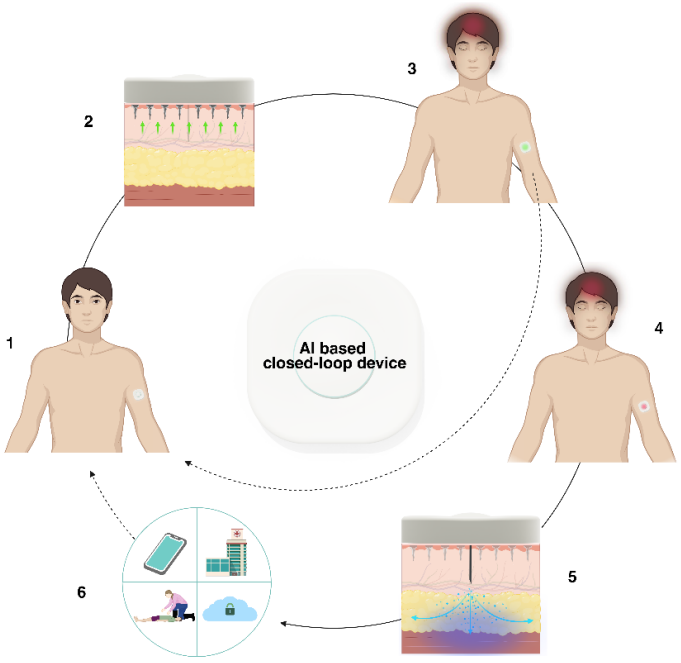

Figure 4.2 – Automated prediction and prevention of SUDEP. The AI-CLD collects ISF via microneedles, analyses biomarker data in real time, and intervenes automatically to prevent SUDEP while communicating risk assessments to CGs and healthcare providers

alert first responders (CGs and healthcare providers), thereby enabling a coordinated and timely response. The mobile app continuously displays the current risk score, tracks changes in the score over time, and shows trends in risk (e.g., increasing or decreasing risk) with corresponding timelines. Additionally, a secondary app provides users with detailed information about their risk profile and uploads data to a secure cloud platform for easy access by the medical team (Figure 4.2 – action 6). Through this platform, healthcare providers can monitor the patient's risk progression and tailor preventive treatments as necessary, ensuring a personalized approach to SUDEP risk management.

2.2. Consumer Involvement in the Project

Realizing the importance of user-centered design in the AI-CLD development process, the NEUROSENSE Consortium has initiated a structured series of workshops to assess PWE and CG's perspectives. The first cross-sectional survey workshop, the results of which have been reported previously [16], identified key values that were incorporated into the preliminary design of the intended AI-CLD prototype (Figure 4.1). Building on these findings, we conducted a second workshop to assess how PWEs and CGs perceive these values in the proposed design. A grounded theory methodological orientation composed of semi-structured interviews and focus groups was used to inductively describe users' perspectives.

Participants were recruited through the Spanish Dravet Foundation and Epilepsy Sparks, which are key contributors to the NEUROSENSE Patient Advisory Board. Both the methods and reporting followed the Standards for Reporting Qualitative Research guidelines [18].

2.3. Focus Group Methodology

Three focus group meetings (two with PWEs and one with CGs) were conducted between October 2024 and February 2025. Two of the meetings took place at El Centro de Referencia Estatal de Atención a Personas con Enfermedades Raras y sus Familias (Creer) in Burgos, Spain, and one was organized online (Zoom Video Communications, Inc, San Jose, CA, USA). Each focus group included six to eight PWEs or CGs, in addition to three members of the research team (J.F., M.F., M.R.) and a facilitator. A total of 8 PWEs and 15 CGs participate. The composition of each focus group aimed to ensure heterogeneity in terms of age, gender, education, and privacy concerns. The latter dimension was regarded as

particularly important because of its potential influence on user's willingness to use wearable AI-CLDs.

A semi-structured interview guide (Appendix S1 and Appendix S2) shaped by literature review and expert insights steered discussions on seizure detection, current monitoring methods, and perspectives on wearable AI-CLDs for SUDEP Prediction and Prevention. During these sessions, PWEs and CGs were offered illustrative materials about the NEUROSENSE project, such as models of the wearable AI-CLD and user instructions (Appendix S4). Participants were actively encouraged to provide their thoughts and opinions on the topics presented by the research team. All interactions were audiorecorded, transcribed verbatim, and translated into English as needed. Possible discussion points were formulated surrounding the use of AI-CLDs and categorized into three main themes (Table S3):

1. PWEs and CGs' attitudes and beliefs related to the prediction and prevention of SUDEP.

2. PWEs and CGs' thoughts and feelings related to the use of closed loop technologies and AI for prediction and prevention of SUDEP.

3. PWEs and CGs' perspectives about using a developed SUDEP predictive and preventive AI-CLD prototype as part of their daily life.

2.4. Data Analysis

A qualitative content analysis with an inductive approach was chosen to describe differences in participants' perceptions according to the methodology developed by Graneheim and Lundman [19]. The text from all focus groups was regarded as one text unit and divided into meaning units, focusing on the manifest content close to the text [19]. The meaning units were condensed into codes which were sorted and abstracted into subcategories based on similarities and differences. The subcategories were then abstracted to categories. The analytic process contained a back and forth movement between the original text and its parts. The trustworthiness of categories and subcategories was strengthened by continued discussions within the full research group. Throughout this process, the group affiliation of the meaning units was kept identifiable to allow description of similarities and differences between groups of participants within each subcategory.

2.5. Ethical considerations

This study was conducted according to the principles of the Helsinki Declaration. The study protocol was evaluated and approved by the Ethics Commission of the Instituto de

Investigação e Inovação em Saúde da Universidade do Porto (i3S). All participants provided written informed consent.

3. Results

The questions used to assess perspectives of PWEs and CGs are listed in Appendix S1 and Appendix S2, respectively. Key findings are summarized in the sections below, whereas representative comments from PWEs and CGs for each of the main theme categories and subcategories are listed in Table S3. Additional details of summary results reporting are provided in Appendix S3.

3.1. Expectations of AI driven AI-CLD in SUDEP Prediction and Prevention

Both CGs and PWEs demonstrated a generally positive attitude toward an AI-based monitoring system for SUDEP prediction and prevention. Most participants expressed comfort with a wearable device (CG Question 1: n=11 comfortable, n=3 very comfortable; PWE Question 1: n=3 comfortable, n=3 very comfortable). However, attitudes toward an implanted version were more variable, with most participants expressing discomfort (Question 3: n=6 CGs and n=4 PWEs) and fewer reporting high comfort levels (Question 3: n=4 CG and n=2 PWEs).

Participants expected the device to provide vital sign information after seizures (Question 17d: n=14 CGs and n=8 PWEs agreed or strongly agreed) and track SUDEP risk over time (Question 17e: n=15 CGs and n=8 PWEs agreed or strongly agreed).

Automatic data sharing with healthcare providers was widely accepted (Question 9), with all CGs and PWEs supporting it in some form. Users cited benefits such as improved medical oversight, increased safety, and real-time medical updates. Participants emphasized that the device should complement healthcare professionals rather than replace them (Question 17h: n=15 CG, n=8 PWEs).

Participants strongly supported features that track SUDEP risk progression over time (Question 17e: n=15 CG, n=8 PWEs agreed or strongly agreed) and provide instant feedback before a seizure (Question 16a: n=15 CG, n=7 PWEs agreed or strongly agreed) as well as before an automated intervention (Question 16b: n=14 CG, n=8 PWEs agreed or strongly agreed)

3.2. AI, SUDEP, and the Decision-Making Process

Both CGs and PWEs had a positive perspective on AI-based SUDEP monitoring, with 11 out of 15 CGs and 6 out of 8 PWEs feeling comfortable or very comfortable with AI tracking SUDEP risk (Question 11). However, both CGs and PWEs raised some concerns over the limitations of AI-driven monitoring, namely the fear of the potential replacement of the human medical decision. Additionally, both CGs and PWEs emphasized that AI-driven interventions should be transparent, and a clear rationale should be provided to enhance trust in the device.

Accuracy was a key consideration. Eight CGs were willing to accept false alarm rates as high as 10%, while others were open to rates of up to 40%. In contrast, PWEs were generally more cautious, with most preferring no false alarms or a tolerance of no more than 5% (Question 12c). The introduction of automatic intervention (e.g., drug administration) generated mixed reactions. While most CGs were open to the concept (Question 17a: n=5 strongly agreed, n=8 agreed), two expressed hesitance. In contrast, all PWEs supported automatic intervention. Control over interventions was another major theme, with all CGs and 6 out of 8 PWEs stating they wanted the ability to adjust interventions (Question 12d).

Concerns were also raised about the safety and reliability of interventions, with 11 CGs and 5 PWEs citing these concerns (Question 12a). Additionally, CGs emphasized the importance of interventions being tied to risk detection of a confirmed SUDEP risk biomarker (Question 17b: n=13 agreed or strongly agreed).

3.3. Barriers and Facilitators to the Adoption and Use of an AI-CLD

Both CGs and PWEs found the wearable prototype acceptable (Question 14a: 11 CG strongly agreed, 4 agreed; 6 PWEs strongly agreed, 2 agreed). Preferences for device placement varied. Most CGs preferred the back (n=10 voted as first choice), while PWEs preferred the arm (n=5 voted as first choice). Wearability factors such as comfort (Question 14c: n=13 CG and n=8 PWEs agreed or strongly agreed) and discretion (Question 14b: n=13 CG and n=7 PWEs agreed or strongly agreed) were largely favoured among both groups. Concerns were raised about the device affecting daily routines, particularly among CGs (Question 14d: n=5 CG and n=2 PWEs agreed).

Regarding interface preferences, CGs favoured mobile phone interaction, while PWEs preferred an integrated screen (Question 6: n=13 CG preferred mobile phone interaction; n=5 PWEs preferred an integrated screen). A mobile app for notifications was strongly

favoured (Question 16i-ii: n=15 CG and n=7 PWEs agreed or strongly agreed), reinforcing the preference for digital integration.

Regarding device replacement frequency, weekly replacements were considered inadequate by most CGs (Question 15b: n=7 disagreed, n=3 strongly disagreed), whereas bi-weekly replacements were seen as more acceptable (Question 15c: n=5 strongly agreed, n=6 agreed). On the contrary, PWEs preferred weekly replacements (n=8 agreed or strongly agreed) over bi-weekly replacements (n=6 agreed or strongly agreed).

Most participants preferred the device to alert them in case of any seizure rather than only those leading to SUDEP (Question 8: n=8 CG and n=7 PWEs), although some supported alerts for both. Nearly all participants wanted alerts if the device became detached unintentionally (Question 16g: n=15 CG and n=7 PWEs agreed or strongly agreed to send alerts to the CG; Question 16h: n=10 CG and n=6 PWEs agreed or strongly agreed to send alerts to the medical team).

Real-time alerts for seizures and device interventions were widely supported, reinforcing the need for a robust communication system (Question 17e: n=15 CG, n=8 PWEs agreed or strongly agreed).

4. Discussion

This study is the first to introduce the concept of a wearable AI-CLD for SUDEP prediction and prevention, and to explore the perspectives of PWEs and CGs on its potential implementation. Our findings indicate a shared general positive attitude and willingness to accept a wearable AI-CLD, with key considerations emerging around device usability, comfort, and control over automated interventions.

The participants recognized the complexities involved in accurately predicting and preventing SUDEP and showed interest in the potential advantages of wearable AI-CLD able to identify a life-threatening seizure and offer an automated immediate intervention. These findings align with the needs, highlighted in the literature, to provide a real-time intervention while minimizing human error [15].

While AI-CLDs have been widely adopted and hailed as a technological revolution in the treatment of people with type 1 diabetes [20], their application to predict and prevent SUDEP represents a novel concept. This may explain why participants' positive views were

contingent on proactive oversight to mitigate potential harms from an automated intervention. While participants were able to appreciate the wide-reaching impact of AI in predicting a life-threatening seizure and preventing SUDEP, both PWEs and CGs emphasized the need to retain control over interventions, as well as the need for more information on how AI might result in harm to them personally, or to those they care about. Specifically, concerns were raised about potential side-effects of a preventive intervention, in line with literature reports highlighting unease about AI replacing users' own decision-making in health-related tasks [21]. Compared with PWEs, CGs were more open to automatic interventions. This may be attributed to differences in risk perception, with CGs prioritizing immediate response capabilities and PWEs being more concerned about autonomy, one of the core principles of medical ethics [22].

While retaining control over interventions may be challenging in emergency scenarios where immediate action is crucial to save a person's life [15], developing interventions with minimal side effects and high safety would be crucial to enable broad acceptance of automated solutions for SUDEP prevention. In addition, to foster trust and encourage adoption, AI-CLDs should be integrated into healthcare in a transparent and informative manner that addresses concerns among PWEs and CGs. A key factor in this integration is the central role of medical teams in medical decision-making, due to broad recognition that physician oversight is essential for patient safety [23]. This aligns with our findings, which highlight the willingness of both CGs and PWEs to share device-generated data with healthcare providers, thereby acknowledging the potential benefits of AI-enhanced medical supervision. Previous studies have shown that digital health interventions can improve patient confidence and support clinical decision-making [24]. The strong support for automatic data transmission further underscores AI's potential to bridge gaps in epilepsy care by enabling real-time communication between PWEs, CGs and healthcare professionals.

An important finding from this study is that both CGs and PWEs exhibit a strong preference for AI-driven wearable devices over implantable solutions. While the majority of participants were comfortable with wearable technology, the notion of implantable AI monitoring received mixed reactions, with many expressing discomfort. Prior research also suggested that non-invasive monitoring is generally more acceptable in epilepsy management, due to concerns about procedural risks and long-term impacts of implantation [25]. The preference for a wearable device highlights the importance of designing non-intrusive, effective monitoring solutions that ensure adherence and acceptance while

integrating seamlessly into daily life. Similar findings emerged from our previous research [16]. User-friendly technology might be particularly beneficial for chronic conditions as it could help to reduce the stigma burden.

Another important finding relates to users' attitude about device specificity, sensitivity and accuracy. Compared with PWEs, CGs expressed a higher tolerance for false alarm rates, probably due to CGs prioritizing comprehensive risk detection and PWEs being more concerned with disruptions to daily life. These results suggest that customizable alert settings may be beneficial in optimizing user's experience, allowing individuals to adjust the sensitivity based on personal preferences.

From a practical standpoint, our findings are important for a successful implementation of AI-based SUDEP risk monitoring. Device discretion, comfort, and usability emerged as significant factors influencing acceptance. Given that most participants favored mobile phone integration over standalone screens, the ultimate design should emphasize seamless digital integration through smartphone applications. Concerns regarding device placement and replacement frequency indicate that flexible options should be explored to cater to diverse user preferences.

Significance for Epilepsy Understanding and Treatment

The results of our study are relevant to ongoing research addressing the unmet need for SUDEP prediction and prevention. Wearable AI-CLDs offer an opportunity to improve early risk detection and enable timely interventions, potentially reducing mortality rates. AI-driven systems may improve clinical decision-making and individualized treatment plans, as indicated by the strong preference for data-sharing with healthcare providers. Insights into alarm sensitivity, intervention control, and user preferences can guide the refinement of future SUDEP predictive and preventive devices. These devices can be customized to increase PWEs and CGs confidence by implementing user-centered design principles, which will eventually result in wider adoption and improved outcomes. Overall, AI-driven SUDEP monitoring has the potential to revolutionize the treatment of epilepsy by enhancing both patient safety and clinical oversight.

5. Limitations

While this study provides valuable evidence supporting the development of user-friendly AI-based devices for SUDEP risk detection and prevention, some limitations should be

acknowledged. The relatively small size of the focus groups may limit the generalizability of the findings. Moreover, we could not provide participants with a tangible prototype. Lack of direct interaction with an actual device or with simulated AI results might have limited participants' understanding of practical complications. Actual implementation might unearth unanticipated benefits or challenges that could alter their perspectives. Once a prototype is available, issues related to long-term usability will also need to be explored.

Of note, the focus group with PWE was held online, reflecting either participant preferences or logistical constraints. Prior research indicates that, although in-person and video call interviews generally produce similar results, in-person interviews often allow greater depth [26]. Despite this, qualitative interviews performed by video, telephone, and online are valid alternatives and offer an acceptable solution when logistical or budgetary constraints are present [27].

6. Conclusion and Future Direction

This study provides valuable insights into the perspectives of PWEs and CGs regarding the use of AI-CLDs for the prediction and prevention of SUDEP. Both groups expressed generally positive attitudes towards wearable AI-CLDs, particularly appreciating the potential benefits of real-time monitoring, automatic data sharing with healthcare providers, and timely intervention. Moreover, our research underscores the need to address key concerns such as accuracy of AI systems, potential automation over-reliance, and control over interventions to ensure that these devices are deployed in a way that builds trust and fosters acceptance among both PWEs and CGs.

Long-term studies will be needed to establish the real-world effectiveness and safety of AI-based SUDEP prevention technologies, especially in diverse populations. Moreover, understanding the ethical, privacy and psychological implications associated with the implementation of AI-powered health technologies will be vital to promote adoption and enhance usability among both PWE and CGs. Optimizing the collaboration between clinical teams, epilepsy advocacy groups, and technology developers will be essential to ensure AI-CLDs meet both clinical and user needs.

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5.

Conclusion

1. Major findings

This thesis aimed to explore the development of medical devices that are aimed at preventing sudden death in epilepsy (SUDEP), focusing on the need for technological precision and effective user engagement in the development process. It addressed a pressing need in current innovation practice: the general absence of significant, ongoing involvement of persons with epilepsy (PWEs), their caregivers (CGs), and other stakeholders in the development of medical technologies related to epilepsy. This thesis presents evidence, drawn from systematic literature review, empirical investigation, and active contribution within the NEUROSENSE project, that a different approach—grounded in participatory design and ethical responsiveness—is not only viable but also effective and replicable. One of the main findings was presented in Chapter 2, which made a thorough analysis of the literature to determine the extent of user participation in the medical device development (MDD) process for epilepsy treatment. The findings indicated that user involvement is rarely observed during the initial phases of MDD—especially during conceptualization and design. Most interactions, when they occur at all, are confined to the deployment process, when device capabilities are already set, and the moment for valuable input has passed. This thesis overturns that paradigm. As outlined in Chapter 2 and developed across the dissertation, our work illustrates that user participation from the earliest points of MDD is not only possible but extremely fruitful. In this way, we provide a proof of concept that other groups and projects with similar problems can adopt.

In particular, the NEUROSENSE project employed a multi-phase participatory process that engaged users from the very beginning of device design, an approach not reported in the literature examined. The first design thinking workshop was an anchor phase for learning about the emotional, functional, and contextual needs of PWE and CGs. It was not merely exploratory—it served as a source of inspiration and guidance for prototype development. The insights obtained through this first workshop significantly influenced the values and specifications of the first prototype of the AI-based, closed-loop device (AI-CLD). This initial encounter was notably enlightening; by emphasizing comfort, discretion, emotional engagement, and integration in daily life, the prototype was designed to conform to actual demands rather than hypothetical assumptions.

The second workshop, described in Chapter 4, took this a step further. Participants were presented with and provided feedback on the functional and esthetic properties of the prototype, generating a feedback loop less typical of medical device design. Consistency

across workshops is an innovation methodological, addressing one of the essential hindrances identified in Chapter 2: that user involvement is often narrow, superficial, or one-off. Our study demonstrated that longitudinal user interaction is not just feasible but also brings tremendous value to design, trust and acceptability, and perceived usability.

These workshops also overcame other barriers to participation identified in the literature: logistical complexity, design illiteracy among users, and ethical and emotional burden concerns. With careful activities, empathetic facilitation, and multilingual outreach engagement, the NEUROSENSE team demonstrated that even highly emotive topics like SUDEP can be addressed collectively in a manner that respects autonomy and optimizes emotional safety.

Apart from workshops, the survey study in Chapter 3 corroborated these findings. It also highlighted the differing awareness and priorities of PWEs and CGs and how they were reflected in their design concerns. Particularly, CGs prioritized automatic intervention and data sharing, while PWEs were concerned about autonomy, continuous monitoring, and emotional intrusiveness. These results informed the design of the modular structure of the prototype, allowing for variable levels of automation and notification, thus promoting a more flexible and inclusive solution.

Chapter 4 interviews and focus groups provided additional assurance that emotional and moral factors like trust, control, and safety are as vital as technical performance. AI seizure prediction and SUDEP prevention interventions are only acceptable when they are perceived as transparent, trustworthy, and respectful of the user's life experience. Acceptance of the prototype by the participants assured that such systems are welcome when created in partnership, not thrust upon.

These revelations provide a straightforward answer to the significant challenge outlined in the Introduction— the conflict between the potential of autonomous, life-saving interventions and the psychological strain that such systems impose on users. The worry regarding spurious alarms, the stress caused by constant monitoring, and the gravity of the consequences of depending on technology for safety are not ancillary concerns but are central to the efficacy or inefficacy of these devices. This dissertation actively met these difficulties by engaging with the voice of users from the onset. Through iterative engagement, co-design workshops, and structured feedback loops, participants were not just heard; they were given the agency to express their own definitions of safety, control, and acceptability. The technology that emerged from the NEUROSENSE project does not

promise to eliminate uncertainty; rather, it aims to navigate it in a way that is ethical and transparent, with adaptability and emotional resonance built into its very design. Trust here is built not by eliminating complexity, but by involving users in controlling it.

In addition, this project provides a most significant illustration that broad co-creation and intellectual property protection are not always incompatible. Among the most prevalent misconceptions of creating medical technology is that opening up the design process to users jeopardizes competitive advantage or is a threat to confidentiality. The NEUROSENSE project refutes it. Early on, a Patient Advisory Board was called together to advise the project direction and values. Although involving users so early necessitated cautious planning, transparency regarding the project scope and limits prevented the establishment of unrealistic expectations or making false promises. This equilibrium—between inspiration and reality, openness and intellectual property protection—was challenging to achieve but not impossible. It demanded truthful communication, ethical principles, and respect. Above all, it shows other research consortia, start-ups, and medical technology companies that stakeholders can be engaged early and in a genuine way without compromising commercial and legal integrity.

Lastly, this thesis entirely embodies the journey "from the bench to the market." At its inception, it commenced with a biomedical research issue—a need to develop clinically meaningful, predictive biomarkers for SUDEP, identified by preclinical models and translated into a technical solution. Yet the reach of this research extended well beyond laboratory walls. It encompassed the recognition of unmet user needs, the development of prototypes informed by ethical considerations, and a validation process based on actual experiences. Each stage—from biomarker discovery through systems design and public trials—was shaped by the dual demands of scientific validity and user significance. This research crossed not just disciplinary lines but the entire translational continuum, including the step from biomedical discoveries at the "bench" level to the earliest stages of market readiness termed the "market." It offers a replicable model of translational innovation—one that places empathy, inclusion, and ethical integrity on par with technical expertise.

2. Limitations and futures research

Although this thesis presents a solid basis for reconceptualizing SUDEP-related device development, a number of limitations have to be considered.

First, although our systematic review was comprehensive, it was from published, peer-reviewed literature. As discussed in Chapter 2, this is likely to underestimate user engagement in industry-led development where practice is proprietary and not consistently reported. Secondly, variability in reporting format and non-standardised terminology across studies made it difficult to cross-compare.

Secondly, survey research utilized convenience sampling via online media, which may exclude those with restricted web access or lesser degrees of digital literacy, biasing the findings toward more active or more digitally literate groups. This introduces a limitation in generalizability, especially when considering designing for more marginalized groups.

Third, qualitative research was conducted on conceptual prototypes instead of fully functional devices. Although responses from participants were rich and informative, hands-on interaction with hardware and real monitoring systems would provide richer insight in the context of usability, reliability, and everyday challenges.

In spite of these constraints, the model presented in this thesis constitutes a sound basis for further research and practical application. It is suggested that the NEUROSENSE participatory model—which begins with early user engagement, proceeds through iterative co-design workshops, and concludes with prototype testing—be used and experimented with in other areas of medical device development, especially in high-risk, emotionally intense areas such as Parkinson's disease, Alzheimer's disease, or chronic pain.

More specifically, future studies should:

- Investigate longitudinal assessments of SUDEP-targeted devices to determine user trust, adherence, and emotional effect in the long run.
- Expand the user base of NEUROSENSE to healthcare professionals, whose feedback on thresholds for intervention, data interpretation, and clinical responsibility is essential to effective integration into treatment protocols.
- Create formal guidance and toolkits that interpret our research methodology into actionable frameworks for other teams developing critical care devices.

The NEUROSENSE project is fully involved in this specific path. The next stage of development will involve medical practitioners, including neurologists, nursing personnel, and emergency response units, in the co-development of intervention protocols and data

handling procedures. This will ensure that the suggested AI-CLD is not just acceptable to the end-users but also clinically viable, ethically acceptable, and easily integrable into existing healthcare systems. Additionally, regulatory agencies, industry partners, and funding agencies are urged to foster systems that support user participation at all stages of the MDD process. This encompasses the development of mechanisms that validate emotional and experiential data as valuable data in regulatory filing and funding approval processes. In conclusion, this thesis demonstrates that early, ongoing, and ethically mindful user involvement in the design of life-critical medical devices is not merely possible, but revolutionary. By challenging prevailing technocentric paradigms and offering a replicable participatory alternative, this work contributes not only to SUDEP prevention, but to a broader vision of healthcare innovation that is open, compassionate, and human-centered.

6.

Supplementary Data

Supplementary Table S1

Table S1 – Data Extraction Form

Author details	Study Design	Country of the study	Year of publication	Objectives	Stages/phases of the development of medical device	Medical Device

Supplementary Table S2

Table S2 – Stages of MDD, an overview of the findings from the selected research studies

Study, year of publication, country of origin	Objective of the study	Stages/phases of the development of the medical device	Methods used for capturing user perspectives by stages of the medical device lifecycle
Hufford, Glueckauf and Webb (1), 1999, US	To examine differences between the perceptions of adolescents with epilepsy and their parents in regard to comfort, distraction, and therapeutic alliance across 3 different modalities: (a) home-based video-system counseling, (b) home-based speakerphone counseling, and (c) videotaped, office-based counseling.	Deployment	Counseling sessions were conducted // After the assessment interview, each family member separately completed the Issue Severity Scale (ISS), Issue Frequency Scale (IFS), and Priority for Intervention Form of Glueckauf's Family and Disability Assessment System // clients completed the Audiovisual Equipment Rating Scale and the Audiovisual Equipment User Survey and a modified version of the Bond subscale of the Working Alliance Inventory for use in family counseling. They also completed the IPS, ISS, and Issue Change Scale (ICS) after the sixth session.
Zamponi, Rychlicki (2), 2008, Italy	To evaluate the safety and efficacy of vagus nerve stimulation (VNS) in very young children suffering from catastrophic epilepsy and status epilepticus.	Deployment	Quality of life was assessed using the Vineland Adaptive Behavior Scale (VABS) and by an analogical scale of parental satisfaction.
DiIorio, Escoffery (3), 2009, US	To evaluate WebEase, an Internetbased,	Concept	Eligible and interested individuals were scheduled to attend one of three

	theory-driven, self-management program for adults with epilepsy.		orientation sessions. At the beginning of the session, the participants completed an online pre-test about medication taking, stress and sleep. Following the survey, study staff presented an introduction to the WebEase Internet site. The participants were able to ask questions and test different components of the program using their own computer during orientation.
Schulze-Bonhage, Sales (4), 2010, Germany, Portugal	To report on a two-center survey of patients ´ views on the practical implementation of seizure prediction devices	Concept	41 outpatients were asked to complete a survey designed to assess their views on the role of unpredictability of seizures, seizure prediction, requirements for the performance of prediction algorithms, and practical aspects of implementation
Koo, Yang (5), 2012, South Korea	To characterize epilepsy patients who use 'Epilia' as a main source of information compared to those who do not use 'Epilia,' but instead rely on healthcare providers for epilepsy-related information. The impact of using 'Epilia' on satisfaction and attitude toward epilepsy was also investigated.	Deployment	Separate surveys were administered to the online and offline groups to investigate their socio-demographic, epilepsy-related, and psychological characteristics, as well as attitude alterations after beginning to use 'Epilia'.
Vonhofen, Evangelista and Lordeon (6), 2012, US	To discuss the implementation of an automated injection system for isotope administration and its impact on staffing, safety, and nursing satisfaction.	Testing & Trials	The postimplementation satisfaction survey was sent to a cohort of 15 staff nurses
Thygesen and Sabers (7), 2013, Denmark	To evaluate the effect of VNS on seizure frequency and to investigate patient satisfaction of and quality of life effects of VNS treatment.	Deployment	The study was an investigator-initiated retrospective survey of patients operated with VNS implantation during a ten-year period.

Brunnhuber, Amin (8), 2014, UK	To describe the development and implementation of video EEG telemetry (VT) in the patient's home (home video telemetry, HVT) in a single centre.	Testing & Trials	We used surveys to survey the principal stakeholders. consultants and technicians), to explore how HVT was perceived.
Askamp and van Putten (9), 2014, The Netherlands	We surveyed Dutch neurologists and patients and evaluated a novel mobile EEG device (Mobita, TMSi).	Deployment	Members of the Dutch Neurological Society were invited to participate in our online survey about the use of EEG in (suspected) epilepsy patients.
Hoppe, Feldmann (10), 2015, Germany	To explore attitudes and preferences towards future devices for seizure detection in adult patients with therapy-refractory epilepsies.	Concept	30-minute semi-structured interview on automated seizure registration
van Andel, Leijten (11), 2015, Denmark	To describe stakeholders and their moral values that are relevant to the development and use of the seizure detector and present four design choices and the corresponding risks and benefits in terms of the identified values.	Testing & Trials	Consortium Meetings, telephone conferences, email communications, survey
Van de Vel, Smets (12), 2016, Netherlands	To compare user experiences with systems for seizure detection, their opinions on usefulness and purpose of seizure detection, and their requirements for such a device.	Deployment	2 Validated surveys: one for patients and caregivers and another for medical doctors
Newman, Shankar (13), 2016, UK	To develop and implement an eHealth solution to support education and self-management of risks, in epilepsy.	Design, Test & Trials	Usability testing: user journeys, user observations, feedback, outcomes, app content evaluation
Patel, Moss (14), 2016, US	To inquire on detection device features that are important to patients and their caregivers.	Concept	A survey instrument
Sauro, Holroyd-Leduc (15), 2016, Canada	To develop a web-based, evidence-informed clinical decision tool to help physicians determine which patients are appropriate for an epilepsy surgery evaluation.	Deployment	Usability testing, focus groups, semi-structured interviews
Tovar Quiroga, Britton and Wirrell (16), 2016, US	To assess persons with epilepsy (PWE) and caregivers' perspectives regarding the features and priorities that should be considered in the design of seizure detection devices	Concept	Survey

Modi, Schmidt (17), 2017, US	to develop an individually tailored intervention, called Epilepsy Journey, to improve aspects of executive functioning through an iterative, patient-centered process including focus groups and usability testing.	Design	The unique needs of adolescents with epilepsy and their families were assessed based on focus groups. In the second phase, the web-based Epilepsy Journey problem-solving intervention was designed, developed, and evaluated. Evaluation took the form of multi-modal usability testing
Ali, Elsayed (18), 2017, US	In a novel approach, we used social media to contact patients with DS to gather data on post-surgical seizure reduction and overall satisfaction with VNS	Deployment	A survey consisting of 10 questions was posted to a social media webpage for a DS support group moderated by the Dravet Syndrome Foundation. The results were analyzed, and percentages reported using the integrated SurveyMonkey analytical software.
Halford, Sperling (19), 2017, US	To evaluate the performance and tolerability in the epilepsy monitoring unit (EMU) of an investigational wearable surface electromyographic (sEMG) monitoring system for the detection of generalized tonic–clonic seizures (GTCSs).	Testing and Trials	A device usability survey was given to subjects.
Ozanne, Johansson (20) 2018, Sweden	To explore perceptions regarding the use of wearable technology in disease monitoring and management as reported by individuals with epilepsy.	Deployment	Focus Groups and semi-structured interviews
Arends, Thijs (21), 2018, Netherlands	To develop and prospectively evaluate a method of epileptic seizure detection combining heart rate and movement.	Testing & Trials	Survey (caregiver) and usability testing (PWE)
Afra, Bruggers (22), 2018, US	To evaluate the patient's interest in using a mobile app for seizure control and self-care.	Concept	Survey
Meritam, Ryvlin and Beniczky (23),	To assess the performance, applicability, and usability of the	Deployment	Post-Study System Usability Survey (PSSUQ), telephone interviews

2018, Denmark	device in home environment of patients		
Janse, Dumanis (24), 2019, US	To promote user-centered design of future seizure forecasting devices by quantifying patient and caregiver preferences for the potential benefits and risks of seizure forecasting devices.	Concept	Best-worst scaling (BWS) survey method
Chiang, Moss (25), 2020, US	To evaluate the association between seizure detection device usage and HR-QOL in an enriched population of SeizureTracker.com electronic seizure diary users.	Deployment	cross-sectional survey
Bruno, Biondi (26), 2020, UK	To assess the self-mastery performance and associated factors in a group of PWE admitted to an epilepsy monitoring unit who agreed to wear a wrist-worn device aimed at seizure detection	Deployment	Usability tests of the wearable device + Wearable technology Self-management Score (WSS)
Bruno, Biondi (27), 2020, UK, Germany	To identify the device placement-related issues experienced by a cohort of people with epilepsy (PWE) to investigate to what extent available devices are nonintrusive, comfortable, and stable on the body.	Deployment	Usability tests of the wearable device + Participants' experience was assessed using the Technology Acceptance Model Fast Form (TAM-FF) plus two additional questions on comfort. A thematic analysis was also performed on the free text of the survey.
Khan, Peechatka (28), 2020, US	To assess patient perceptions of completing ePROs, expectations of ePRO devices for PCOR and on-site clinical visit in order to guide the development of successful ePRO deployment in seizure-related disorders.	Concept	Online survey
Beck, Simony (29), 2020, Denmark	To provide insights into patient readiness to use wearables for home monitoring of epilepsy	Deployment	Semi-structured qualitative interview 8 PWEs.
Thompson, Goodwin (30), 2020, US	Gain the perspectives of transition-age youth with epilepsy (TAYWE), their caregivers, and clinicians to inform the design of a mobile health (mHealth) system to	Deployment	Individual semi-structured interviews (Clinicians) and focus groups (PWE and caregivers)

	support the self-management needs of TAYWE.		
Simblett, Matcham (31), 2020, UK	To conduct a consultation exercise on the clinical end point or outcome measurement priorities for Remote Measurement Technologies studies, drawing on the experiences of people with chronic health conditions.	Concept	Focus Groups
Simblett, Biondi (32), 2020, UK	Assess the first-hand experiences of people with epilepsy using wearable devices, continuously over a period of time. Understand how acceptable and easy they were to use, and whether it is reasonable to expect that people will use them.	Deployment	Semi structured interviews, Usability Test.
Yoo, Lim (33), 2020, South Korea	To develop a mobile epilepsy management application covering crucial factors comprehensively in a user-friendly way.	Design	Scenario-based usability test, satisfaction survey, and interview.
Nasseri, Nurse (34), 2020, UK, US, Germany, Australia	The present study addresses both of these problems of measuring device signal quality and assessing the preferences of people with epilepsy while using wearable devices.	Deployment	At the end of the recording period, patients were provided with a survey to assess their preferences and comfort with using wearable devices for seizure prediction.
Buchhalter, Scantlebury (35), 2021, Canada	Describe the development of the Pediatric Epilepsy Outcome-Informatics Project (PEOIP) at Alberta Children's Hospital (ACH)	Testing and Trials	Meetings (HP), Survey (HP, CG)
Grzeskowiak and Dumanis (36), 2021, US	To understand the use-cases that best suit the needs of epilepsy community as seizure forecast research advances. These results will provide researchers with insight into user-acceptance of using a forecasting tool and incorporation into their daily life. Ultimately, this input from people living with epilepsy and caregivers will provide timely feedback on what the community needs are and ensure researchers and companies first and foremost consider these	Concept	A seizure forecasting survey targeted to those living with epilepsy and their caregivers was generated using Qualtrics (Provo, Utah) and distributed online

	needs in seizure forecasting tools/product development.		
Cote, Beaudet (37), 2021, Canada	To evaluate the extent of utilization and acceptability of a web-based intervention among PWE	Testing and Trials	Pilot parallel-group randomized controlled trial 75 PWE who had Internet access allocated on a 1:1 ratio into an experimental group that received the intervention (experimental group (EG), n = 37) and a control group invited to consult epilepsy-related websites (control group (CG), n = 38).
Bruno, Biondi (38), 2021, UK	To capture focal onset seizures with motor manifestations with a multimodal wearable device to identify the digital semiology and the evolution pattern of ictal manifestations.	Testing and Trials	Participants were asked to wear a multimodal wearable device (IMEC) aimed at seizure detection while admitted to an epilepsy monitoring unit. Seizures were labelled by a neurologist and start, and offset time were noted. The signals captured by the device during the seizure window were plotted and a visual inspection was performed for focal motor seizures with impaired awareness and for focal motor aware seizures
Herrera-Fortin, Bou Assi (39), 2021, Canada	To detail the preferences, needs and concerns regarding potential seizure detectors, of PWE and their caregivers across Canada.	Concept	Two online surveys were designed to survey PWE and their caregivers on seizure detection acceptability and to collect general clinical characteristics.
Olsen, Nielsen (40), 2021, Denmark	To explore the experiences of people with epilepsy using wearables for home seizure monitoring.	Deployment	Usability tests for 3 wearable devices, and semi structured open-ended individual interviews before and after home monitoring with wearable seizure monitoring equipment.

Willems, Baier (41), 2021, Germany	Satisfaction with and reliability of in-hospital video-EEG monitoring systems in epilepsy diagnosis - A German multicenter experience.	Deployment	Survey using a survey to assess the reliability, customer satisfaction, and potential for general or specific improvements of Video-electroencephalography monitoring systems
Monfort, Poulet (42), 2021, France	This exploratory study aims to identify patient and caregiver groups, according to acceptability factors.	Concept	The 31-item Quality of Life in Epilepsy (QOLIE-31) scale, adapted from the more comprehensive 89-item scale; the 10 items Modified Computer Self Efficacy Scale (MCSES). The perception of the occurrence of seizures was evaluated using a Likert scale that ranged from 0 (never) to 5 (once or several times a day, every day). A 21-item survey derived from the UTAUT 2 model was used to determine the connected patch acceptability.
Chiang, Moss (43), 2021, US	Investigate patient and physician perspectives on effective translation of algorithm outputs into data visualizations through health information technology.	Design	We surveyed 627 people living with epilepsy and caregivers, and 28 epilepsy healthcare providers. Respondents scored each visualization in terms of international standardized software quality criteria for functionality, appropriateness, and usability.
Sabers, Aumuller-Wagner (44), 2021, Denmark, Norway, the Netherlands, Belgium	To explore potential clinical benefits of ta-VNS and to evaluate adaptation, compliance, as well as the usability of the device from a service design perspective.	Deployment	Service Design Survey on Medical Devices Used to determine if there were lifestyle and usability issues

Siegel, Johnson (45), 2021, US	To develop clinical decision support to reduce inappropriate prescription of carbohydrate-containing medications in hospitalized children on ketogenic diet.	Testing and Trials	Usability testing recommended by the National Institute of Standards and Technology: formative and summative testing
von Wrede, Rings (46), 2021, Germany	We developed an examination schedule to probe for immediate taVNS-induced modifications of large-scale epileptic brain networks and accompanying changes of cognition and behaviour.	Deployment	Survey on the evaluation of the device. Seven ordinal questions were asked concerning handling, possibility to continue activities while using the device, feeling while using the device, comfort, suitability for long-term and repeated use.
Hadady, Klivenyi (47), 2022, Hungary, Denmark	Evaluate direct user experience with wearable seizure detection devices in the home environment.	Deployment	Structured online survey (175 caregivers and 67 persons with epilepsy)
Schmidt, Glaser (48), 2022, US	To describe the iterative design, development, and evaluation of a novel mHealth learning environment for parents of children with epilepsy.	Design	Preparation included developing user personas and conducting focus groups. Phase 1 used empathy interviews, empathy mapping, and persona development methods. Usability and user experience methods were used, including SME reviews, cognitive walkthroughs, and usability testing. Survey responses and usability feedback were used to further refine the intervention.
Lazaro, Alvaran (49), 2022, South Korea	To develop a mHealth application for seizure management based on the human system integration (HSI) approach.	Concept, Design, Test & Trials	In the first phase, the needs were identified by conducting exploratory interviews with all the relevant stakeholders via e-mail or messaging app. In phase 2, to determine the system requirements, use

			case scenarios were employed wherein narratives or storyboards are created. As a supplement, personas and journey maps were also created to represent target users and their experiences. In the second phase, to determine the system requirements, use case scenarios were employed. In phase 3 a series of prototypes were created and tested. Users were also instructed to download and test the SeeSure app. The proposed app's function was evaluated through a focused-group interview involving the concerned stakeholders (1 PWE, 2 primary caregivers, 1 medical doctor)
Macea, Bhagubai (50), 2023, Belgium	To report the performance of an electroencephalogram (EEG) seizure-detector algorithm on data obtained with a wearable device (WD) in patients with focal refractory epilepsy and their experience.	Deployment	Patients used a WD, the Sensor Dot (SD), to measure two channels of EEG using dry electrode patches during pre-surgical evaluation and at home for up to eight months. An automated seizure detection algorithm flagged EEG regions with possible seizures, which we reviewed to evaluate the algorithm's diagnostic yield. In addition, we collected data on usability, side effects and patient satisfaction with an electronic seizure diary application (Helpilepsy®).
van Leeuwen, Droger (51), 2023, Netherlands	To explore the perspectives of those receiving secondary care on nocturnal SDDs and epilepsy in general.	Concept	Interviews and Surveys

Guerrero-Aranda, Friman-Guillen and González-Garrido (52), 2023, Mexico	To assess the end-users acceptability of this proposed EEG report format.	Deployment	A 16-item electronic survey was sent to physicians who use EEG services of a medical diagnosis clinic.
Lewis-Fung, Tchao (53), 2023, Canada	Design and evaluate the feasibility of VR exposure therapy to treat epilepsy-specific interictal anxiety.	Design, Testing & Trials	online and in-person focus groups and survey
Tchao, Lewis-Fung (54), 2023, Canada	To explore and validate scenarios that provoke epilepsy/seizure-specific (ES) interictal anxiety and provide recommendations that lay the foundation for designing VR-ET scenarios to treat this condition in PwE.	Concept	The survey included open- and closed-ended questions intentionally created to collect information useful for informing the design of VR-ET scenarios for PwE
Lennard, Newman (55), 2023, UK	To evaluate the clinical utility and acceptability of Event Labs seizure monitoring (Nelli) in people with intellectual disability and epilepsy.	Deployment	A survey was developed by the clinical team in discussion. with experts by experience identifying preemptively what the key areas of inquiry need to be on the impact of Nelli.

Supplementary Table S3

Table S3 – Overview of categories, subcategories and representative quotes based on results from the focus groups of PWEs and CGs

Categories	Subcategories	Quotes
Expectations of AI CLD in SUDEP Prediction and Prevention	Attitudes Toward AI-Based Prediction and Prevention of SUDEP	PWE "If I travel alone, and in case a seizure occurs, a wearable device managed by AI would help with an automatic intervention." PWE "As long as the AI is strictly set up and controlled correctly, fine." PWE "Not sure as it is a new concept. I don't really know how safe it would be." PWE "No, I don't have any concerns with an automated intervention as the device purpose is the prevention of SUDEP." PWE "Depends on the risks of the medication if administered as a result of a false positive." CG "As long as it's something that does not threats the health of the person under my care." CG "It might get it wrong once, but as long as it is very well tested and it does not make many mistakes, then it's fine for me." CG "I would not tolerate a compulsory administration of a drug very easily. If, in the other hand, it just sends a notification, I would be more at ease with the use of the device because a false positive would be more acceptable. However, if the administration of a drug is compulsory, I wouldn't be very comfortable." CG "I'm concerned due to the lack of knowledge of this technology. But if I can see it and it proves to be reliable, it would be a good thing."
	Preferred Features and Functions of the AI-CLD	PWE "It seems to me like a good system would have something like this that could just literally administer standard "anti-epileptic" drugs." PWE "I think it would be very nice if both me and my wife could get the notification." CG "The device should be sufficiently intelligent and give parents the power to decide whether or not to administer medication, i.e., it should be configurable."

		CG “Give parents the opportunity to configure when the device alerts you that there is a SUDEP event. Allow us a few moments to administer the drug. If that doesn’t happen then let the device act.”
	Integration with Healthcare Professionals	PWE “So I think if like for instance we had a device that could tell automatically if we'd forgotten our medication and send a message to the doctor, that would be helpful for our communication with our doctors. PWE “I'm very comfortable in automatically sharing my data with my neurologist over the internet.” PWE “When the doctors ask questions, you know, they always want to know, when did it start? How long was it? You know, it's not always easy to remember that. So, if we have something where you can get that actual data or even if you can decide to send that to the doctor.” PWE “Often the caregivers will say understandably their perception of what happened, but it's not necessarily accurate. And so, if you can provide data that not to say you're wrong, but just, you know, something that's more accurate and then you can affect, treat the patient much more effectively.” CG “Being caregivers, we rely very much on our intuition as parents to act properly when needed. This experience no-one else has quite like us.” CG- “I think it's perfect, as the doctor is informed at the same time as we are.”
AI, SUDEP, and the Decision-Making Process	Trust in AI for SUDEP Risk Monitoring	PWE “No one worries if there's a false positive. If all it's doing is kind of keeping you breathing really, but if it's like benzodiazepines or something, then that's a big problem.” CG “I don't think AI has developed enough yet.” CG “If in 15 years this device proves to be reliable, then maybe, little by little, I could delegate some of my responsibilities to it.” CG “I always believe that there must be a human making the decision to administer the drug. A parent's intuition and experience cannot be substituted by AI.”
	Accuracy and Reliability Considerations	PWE “100% accuracy hopefully or as close as possible. No dangers of medication administered in case of false positives.” PWE “Any risk reduction will be good, but hopefully you can get it to be 100%.” CG “The minimum guarantee is that, for example, there aren’t a lot of adverse effects.”

	Control Over AI-Driven Interventions	CG “This way we would retain the power to decide what to do after being notified, just like we have to do now when is our turn to be “ready”. Of course, we can also fail, just like the device, we are only humans. But I would rather be the one failing than trusting the device end then have the device failing on us.” CG “There should be a protocol that warns us when a SUDEP event is happening, giving us, the caregivers, 3 minutes to act and, for instance, press “yes” or “no” on the app notification for drug delivery.”
Barriers and Facilitators to the Adoption and Use of a AI-Driven AI-CLD	Wearability and Usability Factors	PWE “A lot of people probably wouldn't even question it because they wouldn't know that it's not a device for diabetes.” CG “I would like if the device was a bit thinner. Now that I’m handling it, it feels like you could still see it through the clothes. I’m not saying this for aesthetic reasons, but rather because kids will notice it and might try to remove it.” CG “Could be possible to camouflage the device using an appropriate colour, so the user wont even notice it’s wearing it.” CG “The size it doesn't bother me, I would use it, but of course, uncomfortable for them.” CG “I think it's something that would go very unnoticed because a lot of people already wear something similar.”
	System Alerts and Notifications	PWE- “I might not want to see that warning because it might make me feel more stressed or something, I wouldn't really care because SUDEP doesn't scare me at all.” CG - I think the device should also allow the parent to make a decision when notified. Before the decision to administrate is made, could the artificial intelligence automatically ask you if you agree to let them administrate?’ CG - it would be necessary to differentiate when it is a crisis, that is, to somehow know when a crisis is going to happen. That is to say, to differentiate a “crisis” from SUDEP.”

Appendix S1 – Interview Guide Focus Group caregivers (CG)

Aims:

1. Understand caregivers' attitudes and beliefs concerning the prediction and prevention of SUDEP.

2. Understand caregivers' experiences, thoughts and feelings related to the use of digital technology and AI for remote monitoring of SUDEP Risk.

3. Explore the factors that would impact (positively or negatively) caregivers' acceptability of AI-based remote monitoring of SUDEP Risk.

4. Explore the initial thoughts for using a developed SUDEP predictive and preventive medical device prototype as part of their daily life.

General Instructions

1. Conducting the interviews

1.1. **Present** yourself and **thank** for participation in advance:

"Good morning and welcome to our interview. Thanks for joining us to talk about the use of remote monitoring and artificial intelligence in SUDEP prediction and prevention. My name is [*say your name*], and I am a researcher at XXXX. This interview is estimated to take 1 hour"

1.2. Explain **shortly** purpose of the interview:

Briefly explain the **aim** of the project: "Within the NEUROSENSE project, we aim to develop artificial intelligence solutions to predict and prevent SUDEP. We aim to assist in developing medical device prototypes by applying methods that involve both persons with epilepsy, caregivers and clinicians."

Briefly explain how the **results** will be used: "The results will help to create intelligent medical devices using artificial intelligence that can detect a possible life-threatening seizure and automatically start an intervention to prevent SUDEP. By talking with you, we will be able to develop solutions that persons with epilepsy accept, trust and use."

Briefly explain **people's selection** for the interview: "We selected caregivers for this focus group."

1.3. Put interviewee at ease:

- We will call each other by the first name, if you want to be called by the last name let us know.
- Your responses will be treated confidentiality.
- Your names will be removed from the transcriptions and will not be used in any report.
- The focus group will last approximately one hour to 90 minutes.

- Your participation is voluntary, you do not have to answer anything you do not feel comfortable answering. You can stop the interview at any time, without having to give a reason.
- There are no right or wrong answers, only differing points of view.
- Please, feel free to share your point of view.
- You don't need to agree with others, but please listen respectfully as others share their views.
- The interview audio will be digitally recorded. The session will be recorded to ensure we hear and understand all your comments. To enable this, we kindly ask that only one person speaks at a time.
- Finally, rules for cell phones apply. Please turn off your phones. If you cannot and if you have to answer a call, please do it as silently as possible and join us as soon as possible.

1.4. The focus group guide includes questions at multiple levels

- Each of the questions marked with numbers (e.g., 1.; 2.) should be posed during the focus group.
- Sub-questions marked with letters (e.g., a.; b.) need to be addressed. However, if the subject is already discussed after posing the main question, the question does not need to be asked explicitly.
- Probes are merely provided as conversation starters and do not need to be covered.

2. Start the recording.

3. Begin the Interview

Part 1 - Questions regarding the progression of the condition and the current clinical assessment for Epilepsy severity

Aim: To understand CGs experiences with current Epilepsy management. No need to record the answers

1. Could you describe how the condition of the person you take care of is currently followed?

Probes: Where? How often? By whom?

Part 2 - Questions regarding remote monitoring and AI for SUDEP Prediction and Prevention

Aim 1: To understand CGs experiences with remote monitoring.

Now, we will ask you some questions related to the use of wearable devices. Wearable devices, known mostly just as "wearables," are electronic devices that you can use to track the number of steps you make in a day or to measure things like your heart rate or sleep. An example of a wearable often seen is a 'smartwatch'. These are watches that in addition to providing the time, register movements such as the distance you've walked or your temperature. Popular providers of these smartwatches are for instance Apple and Fitbit. A further step has been taken in the field of medical wearable devices, the so-called closed-loop medical device. A closed-loop medical device is like having a smart assistant that constantly watches over a specific health condition and automatically adjusts treatment without needing an intervention from the user. Let's use the example of a continuous glucose monitoring (CGM) system coupled with an insulin pump to explain this concept in simpler terms. A CGM system constantly tracks blood sugar levels using a small sensor under the skin, while an insulin pump delivers insulin to the body. When these two devices work together, the CGM provides real-time glucose data to the pump, which can automatically adjust insulin delivery to help maintain stable blood sugar levels, reducing the need for manual checks and injections.

In the NEUROSENSE Project, we are designing a closed-loop medical device prototype to predict and prevent SUDEP. These prototypes will be designed to be placed on the skin, where it will collect interstitial fluid. These prototypes will analyse some molecules in the interstitial fluid to understand if a particular seizure could be a potentially life-threatening seizure. Upon the identification of a life-threatening seizure, these prototypes will inject a drug automatically to prevent SUDEP. These prototypes are planned to be connected to your mobile phone, so you can monitor your SUDEP risk autonomously.

Show the NEUROAI prototype and Application Instructions – Power Point

Explain how to apply the sensor and its functions with PowerPoint support

QUESTIONS

1. What do you think about the **size, color, shape** of the NEUROAI Prototype?

No opinion	Very uncomfortable	Uncomfortable	Comfortable	Comfortable, emotionally safe	Very comfortable

2. How comfortable do you feel with the idea of this wearable device placed **on the skin of the person in your care**?

Not an option	Very uncomfortable	Uncomfortable	Comfortable	Comfortable, emotionally safe	Very comfortable

3. How comfortable do you feel with the idea of a smaller device (like a pill-sized device) implanted **under the skin of the person in your care**?

Not an option	Very uncomfortable	Uncomfortable	Comfortable	Comfortable, emotionally safe	Very comfortable

4. What would be the **best part of the body** to wear the device? **Select 3** body parts that you would prefer to place the device the skin of the person in your care, in order of preference.

Arm	Fore Arm	Chest	Belly	Back	Legs	Other (which)

5. According to the instructions, on a scale of 1 (not comfortable) to 5 (very comfortable), how would you feel about **applying the device yourself**?

6. Would you prefer to **have a screen** on the device or interact through the mobile phone?

Yes	No	Maybe

7. How do you think the person in your care would feel about others seeing the device?
8. Would you like the device to warn you in case of any seizure, or only seizures that could lead to SUDEP?
9. How do you feel about automatically sharing your data with your clinic/doctor over the Internet?

Not a good idea	Indifferent	Comfortable	Very Comfortable

10. What do you think about using more than one device?

Not a good idea	Indifferent	Comfortable	Very Comfortable

Aim 2: To describe caregivers' expectations regarding the contribution of AI to the clinical decision-making process

Explain what AI is: Artificial intelligence or AI describes the ability of computers to think like a human. In doing so, computers can assist clinicians in their decision making by processing many types of information simultaneously. A chess computer game is an example of AI. So artificial intelligence can process much more relevant information than the doctor can at a single time. Artificial intelligence could for instance use all the data from your Smart Watch to track your movements and identify problems relating to your disease. If the AI sees anything abnormal, it could notify your doctor or initiate a drug administration.

11. How do you feel about having this wearable device using AI to help you keep track of the SUDEP risk progression of the person in your care (1-Not comfortable to 5- Very comfortable)?

12. Imagine that from the data analysed by the AI, the wearable device would also be able to **promote an intervention automatically** (i.e., administer a drug) to prevent SUDEP without human intervention. What do you think about that?

    a. Do you have any concerns with an automated intervention? (Yes or No and why?)

    b. What are the minimum needs or guarantees for you to accept such an automatic intervention?

    c. Would you accept a drug administration even if there are rare false alarms (thus unnecessary rare drug administrations)? If yes, what is the threshold of rate of false alarms and consequently false interventions you would accept?

1-25%	26-50%	51-75%	76-100%

    d. Would you like to have control over any aspects of the drug delivery system (e.g., the ability to delay or cancel a dose)?

Always (I want control)	Yes	During an experimental phase	Maybe	No	Never (don't want to have that responsibility)

    e. What could be the advantages of the automatic intervention?

Reduction of stress levels and anxiety	Comfort	More independence and safety	None	Other

13. What is the **minimum risk-reduction** of experiencing a life-threatening seizure you would consider sufficient for motivating you to use the device (i.e. 60% risk reduction)?

1-25%	26-50%	51-75%	76-100%

Part 3 – Speed Dating Responses to Likert statements about eh NEUROAI prototype (Strongly agree/ Agree/ Do not Agree or Disagree/ Disagree/ Strongly Disagree)

Aim: To quantify acceptability of NEUROSENSE AI Prototype key aspects.

Wearability of a medical sensing device	Strongly agree	Agree	Disagree	Strongly Disagree
Is it acceptable to use?				
Is it discreet?				
Is it comfortable?				
Wearing the device will affect the daily routines of the person in your care?				
Would it accidentally detach?				

User interface	Strongly agree	Agree	Disagree	Strongly Disagree
Should be accompanied by clear and readable instructions for use?				
Would a weekly replacement be adequate?				
Would a bi-weekly replacement be adequate?				

Wearer interface	Strongly agree	Agree	Disagree	Strongly Disagree
Should give instant feedback to you before a seizure?				
Should give instant feedback before automated intervention?				

Should only monitor the risk of SUDEP?					
Should send alerts to the user?					
Should send alerts to emergency units?					
Should send alerts to caregivers?					
Should a specific alert be sent to the caregivers in case the device is wrongly removed?					
Should a specific alert be sent to the medical team in case the device is wrongly removed?					
How would you prefer to **interface with the device?**	Small green light when active, red light when inactive on the device itself?				
	An app-notification on your phone interface for turning on, stand-by, connecting, notification for active device, notification if the measurement is on-going?				
Would a **non-flashing light for battery replacement** be a good addition?					

Clinical Accuracy	Strongly agree	Agree	Disagree	Strongly Disagree
Would you expect the device to automatically promote an intervention (i.e., administer a drug)?				
Would you accept an automatic intervention, but only when the device recorded dangerous levels of a SUDEP Biomarker?				

Would you expect the device to inform the user if an intervention has been made?				
Should the device inform the caregiver of vital signs at the end of the seizure (i.e. stabilization of vital signs, SpO2, ECG parameters)?				
Should provide you track record of SUDEP risk?				
Would you expect the device to reduce your trips to the hospital, or emergency services?				
Would you like for your medical team to have access to the information as part of your care?				
Could work alongside your medical care team, instead of replacing them?				

Part 4 - Closing

1. Does the second attending interviewer have any questions?

2. Is there anything else you would like to share with us about what we have discussed?

3. Do you have any questions

Appendix S2 – Interview Guide Focus Group persosn with epilepsy (PWE)

Aims:

1. Understand patients' attitudes and beliefs related to prediction and prevention of SUDEP.
2. Understand patients' experiences, thoughts and feelings related to the use of digital technology and AI for remote monitoring of SUDEP Risk.
3. Explore the factors that would impact (positively or negatively) patients' acceptability of AI-based remote monitoring of SUDEP Risk.
4. Explore the initial thoughts for using a developed SUDEP predictive and preventive medical device prototype as part of their daily life.

General Instructions

1. Conducting the interviews

1.1. Present yourself and Thank for participation in advance:

"Good morning and welcome to our interview. Thanks for taking the time to join us to talk about the use of remote monitoring and artificial intelligence in SUDEP prediction and prevention. My name is [*say your name*], and I am a researcher at XXXX. This interview is estimated to take 1 hour"

1.2. Explain shortly purpose of the interview:

Briefly explain the aim of the project: "Within the NEUROSENSE project, we aim to develop artificial intelligence solutions to predict and prevent SUDEP. We aim to assist in developing medical device prototypes by applying methods that involve both persons with epilepsy, caregivers and clinicians."

Briefly explain how the results will be used: "The results will help to create intelligent medical devices using artificial intelligence that can detect a possible life-threatening seizure and automatically start an intervention to prevent SUDEP. By talking with you, we will be able to develop solutions that persons with epilepsy accept, trust and use."

Briefly explain people's selection for the interview: "We selected adults with epilepsy for this focus group."

1.3. Put interviewee at ease:

- We will call each other by the first name, if you want to be called by the last name let us know.
- Your responses will be treated confidentiality.
- Your names will be removed from the transcriptions and will not be used in any report.
- The focus group will last approximately one hour to 90 minutes.

- Your participation is voluntary, you do not have to answer anything you do not feel comfortable answering. You can stop the interview at any time, without having to give a reason.
- There are no right or wrong answers, only differing points of view.
- Please, feel free to share your point of view.
- You don't need to agree with others, but please listen respectfully as others share their views.
- The interview audio will be digitally recorded. The session will be recorded to ensure we hear and understand all your comments. To enable this, we kindly ask that only one person speaks at a time.
- Finally, rules for cell phones apply. Please turn off your phones. If you cannot and if you have to answer a call, please do it as silently as possible and join us as soon as possible.

1.4. The focus group guide includes questions at multiple levels

- Each of the questions marked with numbers (e.g., 1.; 2.) should be posed during the focus group.
- Sub-questions marked with letters (e.g., a.; b.) need to be addressed. However, if the subject is already discussed after posing the main question, the question does not need to be asked explicitly.
- Probes are merely provided as conversation starters and do not need to be covered.

2. Start the recording.

3. Begin the Interview

Part 1 - Questions regarding the progression of the disease and the current clinical assessment for Epilepsy severity

Aim: To understand PWEs experiences with current Epilepsy management. No need to record the answers

1. Could you describe how your condition is currently followed?

Probes: Where? How often? By whom?

Part 2 - Questions regarding remote monitoring and AI for SUDEP Prediction and Prevention

Aim 1: To understand PWEs experiences with remote monitoring.

Now, we will ask you some questions related to the use of wearable devices. Wearable devices, known mostly just as "wearables," are electronic devices that you can use to track the number of steps you make in a day or to measure things like your heart rate or sleep. An example of a wearable often seen is a 'smartwatch'. These are watches that in addition to providing the time, register movements such as the distance you've walked or your temperature. Popular providers of these smartwatches are for instance Apple and Fitbit. A further step has been taken in the field of medical wearable devices, the so-called closed-loop medical device. A closed-loop medical device is like having a smart assistant that constantly watches over a specific health condition and automatically adjusts treatment without needing an intervention from the user. Let's use the example of a continuous glucose monitoring (CGM) system coupled with an insulin pump to explain this concept in simpler terms. A CGM system constantly tracks blood sugar levels using a small sensor under the skin, while an insulin pump delivers insulin to the body. When these two devices work together, the CGM provides real-time glucose data to the pump, which can automatically adjust insulin delivery to help maintain stable blood sugar levels, reducing the need for manual checks and injections.

In the NEUROSENSE Project, we are designing a closed-loop medical device prototype to predict and prevent SUDEP. These prototypes will be designed to be placed on the skin, where it will collect interstitial fluid. These prototypes will analyse some molecules in the interstitial fluid to understand if a particular seizure could be a potentially life-threatening seizure. Upon the identification of a life-threatening seizure, these prototypes will inject a drug automatically to prevent SUDEP. These prototypes are planned to be connected to your mobile phone, so you can monitor your SUDEP risk autonomously.

Show the NEUROAI prototype and Application Instructions – Power Point

Explain how to apply the sensor and its functions with PowerPoint support

QUESTIONS

1. What do you think about the **size, color, shape** of the NEUROAI Prototype?

No opinion	Very uncomfortable	Uncomfortable	Comfortable	Comfortable, emotionally safe	Very comfortable

2. How comfortable do you feel with the idea of this wearable device implanted **on your skin**?

Not an option	Very uncomfortable	Uncomfortable	Comfortable	Comfortable, emotionally safe	Very comfortable

3. How comfortable do you feel with the idea of a smaller device (like a pill-sized device) implanted **under your skin**?

Not an option	Very uncomfortable	Uncomfortable	Comfortable	Comfortable, emotionally safe	Very comfortable

4. What would be the **best part of the body** to wear the device? Select 3 parts of the body that you would prefer to wear the device in order of preference.

Arm	Fore Arm	Chest	Belly	Back	Legs	Other

5. According to the instructions, on a scale of 1 (not comfortable) to 5 (very comfortable), how would you feel about **applying the device yourself**?

6. Would you prefer to **have a screen** on the device or interact through the mobile phone?

Yes	No	Maybe

7. How do you feel about others seeing the device?
8. Would you like the device to warn your caregiver in case of any seizure, or only seizures that could lead to SUDEP?
9. How do you feel about automatically sharing your data with your clinic/doctor over the Internet?

Not a good idea	Indifferent	Comfortable	Very Comfortable

10. What are your feelings about using more than one device?

Not a good idea	Indifferent	Comfortable	Very Comfortable

Aim 2: To described their expectations regarding the contribution of AI to the clinical decision-making process

Explain what AI is: Artificial intelligence or AI describes the ability of computers to think like a human. In doing so, computers can assist clinicians in their decision making by processing many types of information simultaneously. A chess computer game is an example of AI. So artificial intelligence can process much more, relevant information than the doctor can at a single time. Artificial intelligence could for instance use all the data from your

Smart Watch to track your movements and identify problems relating to your disease. If the AI sees anything abnormal, it could notify your doctor or initiate a drug administration.

11. How do you feel about having this wearable device using AI to help you **keep track of your SUDEP risk** progression (1-Not comfortable to 5- Very comfortable)?
12. Imagine that from the data analysed by the AI, the wearable device would also be able to **promote an intervention automatically** (i.e., administer a drug) to prevent SUDEP without human intervention. What do you think about that?
    a. Do you have any concerns with an automated intervention? (Yes or No and why?)
    b. What are the minimum needs or guarantees for you to accept such an automatic intervention?
    c. Would you accept a drug administration even if there are rare false alarms (thus unnecessary rare drug administrations)? If yes, what is the threshold of rate of false alarms and consequently false interventions you would accept?

1-25%	26-50%	51-75%	76-100%

    d. Would you like to have control over any aspects of the drug delivery system (e.g., the ability to delay or cancel a dose)?

Always (I want control)	Yes	During an experimental phase	Maybe	No	Never (don't want to have that responsibility)

    e. What could be the advantages of an automatic intervention?

Reduction of stress levels and anxiety	Comfort	More independence and safety	None	Other

13. What is the **minimum risk-reduction** of experiencing a life-threatening seizure you would consider sufficient for motivating you to use the device (i.e. 60% risk reduction)?

1-25%	26-50%	51-75%	76-100%

Part 3 – Speed Dating Responses to Likert statements about eh NEUROAI prototype (Strongly agree/ Agree/ Do not Agree or Disagree/ Disagree/ Strongly Disagree)

Aim: To quantify acceptability of NEUROSENSE AI Prototype key aspects.

Wearability of a medical sensing device	Strongly agree	Agree	Disagree	Strongly Disagree
Is it acceptable to use?				
Is it discreet?				
Is it comfortable?				
Wearing the device will affect your normal daily routines?				
Would it detach accidentally?				

User interface	Strongly agree	Agree	Disagree	Strongly Disagree
Should be accompanied by clear and readable instructions for use?				
Would a weekly replacement be adequate?				
Would a bi-weekly replacement be adequate?				

Wearer interface		Strongly agree	Agree	Disagree	Strongly Disagree
Should give instant feedback to you before a seizure?					
Should give instant feedback before automated intervention?					
Should only monitor the risk of SUDEP?					
Should send alerts to the user?					
Should send alerts to emergency units?					
Should send alerts to caregivers?					
Should a specific alert be sent to the caregivers in case the device is wrongly removed?					
Should a specific alert be sent to the medical team in case the device is wrongly removed?					
How would you prefer to **interface with the device?**	Small green light when active, red light when inactive on the device itself?				
	An app-notification on your phone interface for turning on, stand-by, connecting, notification for active device, notification if the measurement is on-going?				
Would a **non-flashing light for battery replacement** be a good addition?					

Clinical Accuracy	Strongly agree	Agree	Disagree	Strongly Disagree

Would you expect the device to automatically promote an intervention (i.e., administer a drug)?				
Would you accept an automatic intervention, but only when the device recorded dangerous levels of a SUDEP Biomarker?				
Would you expect the device to inform the user if an intervention has been made?				
Should the device inform the user of vital signs at the end of the seizure (i.e. stabilization of vital signs, SpO2, ECG parameters)?				
Should provide you track record of SUDEP risk?				
Would you expect the device to reduce your trips to the hospital, or emergency services?				
Would you like for your medical team to have access to the information as part your care?				
Could work alongside your medical care team, instead of replacing them?				

Part 4 - Closing

1. Does the second attending interviewer have any questions?

2. Is there anything else you would like to share with us about what we have discussed?

3. Do you have any questions?

Appendix S3 – Tables of responses collected during the focus groups with Persons with Epilepsy (PWE) and Caregivers (CG)

COLLECTED DATA:

S1. What do you think about the size, colour, shape of the NEUROAI Prototype?

	No opinion	Very uncomfortable	Uncomfortable	Comfortable	Comfortable, emotionally safe	Very comfortable
CG	0	0	1	11	0	3
PWE	0	0	1	3	1	3

S2. How comfortable do you feel with the idea of this wearable device placed on the skin of the person in your care?

	No opinion	Very uncomfortable	Uncomfortable	Comfortable	Comfortable, emotionally safe	Very comfortable
CG	0	0	0	6	7	2
PWE	0	0	0	5	1	2

S3. How comfortable do you feel with the idea of a smaller device (like a pill-sized device) implanted under the skin of the person in your care?

	No opinion	Very uncomfortable	Uncomfortable	Comfortable	Comfortable, emotionally safe	Very comfortable
CG	1	2	6	2	0	4
PWE	0	0	4	1	1	2

S4. What would be the best part of the body to wear the device? Select 3 body parts that you would prefer to place the device in the skin of the person in your care, in order of preference.

	Arm	Fore Arm	Chest	Belly	Back	Legs	Other
CG	9	9	4	1	13	8	1
	5x as 1st 3x as 2nd 1x as 3rd	5x as 2nd 4x as 3rd	2x as 2nd 2x as 3rd	1x as 3rd	10x as 1st 1x as 2nd 2x as 3rd	4x as 2nd 4x as 3rd	1x as 3rd
PWE	8	2	1	1	1	0	0
	5x as 1st	2x as 2nd	1x as 3rd	1x as 2nd	1x as 3rd		

S5. According to the instructions, on a scale of 1 (not comfortable) to 5 (very comfortable), how would you feel about applying the device yourself?

	Not comfortable				Very comfortable
CG	0	1	1	3	10
PWE	0	0	2	3	3

S6. Would you prefer to have a screen on the device or interact through the mobile phone?

	Yes, screen on the device	No, interact through the mobile phone	Maybe/Other
CG	0	13	app downloadable on any device both
PWE	5	0	3

S7. How do you think the person in your care would feel about others seeing the device?

CG Open answer:

- Nothing would happen.
- Due to cognitive impairments, he would not mind.
- Nothing would happen. He's used to seeing similar devices. If alright, there won't be a problem.
- No problem.
- This seems to me to be an invasive action.
- Would feel normal, they adapt to everything. Maybe at first, they feel strange, but then they feel good.
- He would not know.
- They wouldn't care.
- We don't care.
- Would not care.
- Would not care.
- Something safer.
- Would not realize it and as a caregiver we couldn't care less.
- Would not care.
- Would feel the same as without device.

PWE Open answer:

- I would just see it as a medical device similar to that used by people with diabetes.
- I'd wear it under my sleeve so no one would see it. But would let family know it is there.
- Fine.
- I would not be uncomfortable.
- It's a nice small device.
- Cool! It's an opportunity to talk about and raise awareness of the epilepsies and SUDEP.
- I think it's a game changer as along as it reduces seizures, I'm very much okay.
- Maybe a little self-aware.

S8. Would you like the device to warn you in case of any seizure, or only seizures that could lead to SUDEP?

	Yes, in case of any seizure	No, only seizures that could lead to SUDEP	Other
CG	8	0	Both: 7
PWE	7	0	Both: 1

S9. How do you feel about automatically sharing your data with your clinic/doctor over the Internet?

CG Open answer:

- I think it's good.
- I wouldn't mind.
- Yes, it would be very interesting if the doctors agree to it.
- I wouldn't have a problem; it would be great if the neurologist or specialist would be aware of it.
- If it's for my son's safety, I think it's perfect. In the case of my son's illness, the more information the doctors receive, the better.
- I think it's perfect, as the doctor is informed at the same time as we are.
- I would have no problem.
- I think it is very good that the doctor can have the information perhaps in the patient's medical record.
- I think it's very good.
- Yes, I would share the data.
- There would be no problem
- Perfect.
- Yes, it's fine if data sharing is optional.
- I totally agree.
- I have no problem.
- Very positive.

PWE Open answer:

- Fine.
- Not sure but ok if necessary.
- Fine.
- Very comfortable as would send information in time while it happens.

- I'm very comfortable in automatically sharing my data with my neurologist through the internet.
- Cool with that - if my data is secure. I wouldn't want anyone bar my clinician to see it though.
- As long as it helps the world and make people with epilepsy better, I'm okay with it.
- Fine, I think it would be a very good idea if the technology is available to the clinicians.

S10. What do you think about using more than one device?

	Not a good idea	Indifferent	Good idea/Comfortable	Very good idea/Very Comfortable
CG	6	1	4	2
PWE	1	0	3	4

S11. How do you feel about having this wearable device using AI to help you keep track of the SUDEP risk progression of the person in your care (1-Not comfortable to 5-Very comfortable)?

	Not comfortable				Very comfortable
CG	0	2	2	5	6
PWE	0	0	2	0	6

S12. Imagine that from the data analysed by the AI, the wearable device would also be able to promote an intervention automatically (i.e., administer a drug) to prevent SUDEP without human intervention. What do you think about that?

CG Open answer:

- I don't know.
- I think it's good.
- There would be no problem, as long as it is safe for the patient and does not cause harm in the event of a false positive.

- If the medication is not going to create a greater harm, there would be no problem.
- The same concern I have about the lack of knowledge of this technology. If I can see it and it proves to be reliable, it would be a good thing.
- I would like to know, and if it doesn't affect the child, I think it's fine.
- There would be no problem if the device administers safe medication that does not affect the child.
- I don't like it.
- I would not allow.
- I always believe that it must be a human decision to administer it.
- A parent's intuition and experience cannot be substituted by AI.
- I would feel comfortable if it was sufficiently proven.
- No answer.
- I believe it is necessary for someone to intervene.
- It sounds very good.
- With the current state of development of AI, I wouldn't be comfortable.

PWE Open answer:

- Unsure.
- Happy if it saves me as I have lost 2 friends to epilepsy.
- Okay.
- That could be positive as it could very well be life saving.
- When I have to travel and seizure occurs, a wearable device managed by AI with automatic intervention would be helpful.
- Depends on the data you can provide me to show accuracy! But overall, yes.
- I think if it works it's okay, but too dependent. Is risky
- As long as the AI strictly set up and controlled correctly, fine.

S13. Do you have any concerns with an automated intervention? (Yes or No and why?)

	Yes	No
CG	11 conditioned to compatibility; lack of confidence; …	4
PWE	5	3

	Unsure; depends if it works or if its trustworthy; Not sure as it is a newer concept regarding AI. I don't really know how safe it would be.; Depends if the drug dopes me up (eg benzo) unnecessarily (false positive). Depends how often this might happen. If this happened a lot I'd probably remove the device to be honest. If the drug didn't have any negative side effects, I wouldn't care about automated or false positives at all.; depending on the risks of the medication if administered as a result of a false positive. For example, with the rescue medication Buccolam, there is a risk of affecting the breathing, but it's used to try to save a life due to a seizure, then it's OK. But if there is a false positive, what would be the dangers to the person from the administration of medicine that is not needed?	

S14. What are the minimum needs or guarantees for you to accept such an automatic intervention?

CG Open answer:

- I agree.
- Robust Clinical Process
- It would be wonderful to be able to configurate the device to the patient's needs in order to administer this medication. If it is harmless, I would have no problem with the administration.
- I would love if the device would allow the parents to set up the device in such a way that in case of high risk of SUDEP we would receive the alert but the device would wait a few seconds and not act, to give us a chance to administer the drug. If we fail to do so, then the device would automatically administrate the drug.
- Compatibility with my child's illness. Guarantees that the device adheres to the safety protocols so that unnecessary administrations are avoided.
- That it does not affect the child. Let me know what has been administered, so that I can find out what has happened and what to do.
- The device should be sufficiently intelligent and give parents the power to decide whether or not to administer medication, i.e., it should be configurable.
- Our control.
- To pass by me
- That it is controlled by me, that I have the final decision on how to administer it.
- That we can be sure it works.
- That it does not have something dangerous in it.
- That it has no serious risks or side effects.
- To have a certain guarantee.

- That the drug only has a positive effect on the patient.

PWE Open answer:

- Unsure.
- I hope it works. I hope it's safe.
- Safety.
- My Neurologist saying it would be safe.
- To live a stress free life.
- Statistical evidence that potential false positives are unlikely.
- 100% accuracy hopefully or as close as possible. No danger with the medication administered in case of false positives.

S15. Would you accept a drug administration even if there are rare false alarms (thus rare and unnecessary drug administrations)? If yes, what is the threshold of rate of false alarms and consequently false interventions you would accept?

	No	5%	10%	20%	40%	60%	80%
CG	0	0	8	2	5	0	0
PWE	1	4	0	0	2	1	0

S16. Would you like to have control over any aspects of the drug delivery system (e.g., the ability to delay or cancel a dose)?

	Always (I want control)	Yes	During an experimental phase	Maybe	No	Never (don't want to have that responsibility)
CG	9	6	0	0	0	0
PWE	3	3	0	2	0	0

S17. What could be the advantages of the automatic intervention?

	Reduction of stress levels and anxiety	Comfort	More independence and safety	None	Other
CG	9	6	5	0	0

PWE	6	4	7	0	0

S18. What could be the problems of the automatic intervention?

	Taking unnecessary chances by trusting too much in AI	Taking unnecessary chances by trusting too much in the delivery mechanism	Other
PWE	4	1	3 False positives Machine jamming Both

S19. What is the minimum risk-reduction of experiencing a life-threatening seizure you would consider sufficient for motivating you to use the device (i.e. 60% risk reduction)?

	10%	20%	30%	40%	50%	60%	75%	80%	100%
CG	1	2	2	2	1	0	1	4	0
PWE	0	0	1	0	2	1	0	1	2

Wearability of a medical sensing device

S20. Is it acceptable to use?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	11	4	0	0
PWE	6	2	0	0

S21. Is it discreet?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	3	10	2	0
PWE	4	3	1	0

S22. Is it comfortable?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	6	7	2	0
PWE	4	4	0	0

S23. Wearing the device will affect your normal daily routines?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	1	5	5	4
PWE	0	2	5	1

S24. Would it detach accidentally?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	5	7	3	0
PWE	0	3	2	3

User interface

S25. Should be accompanied by clear and readable instructions for use?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	7	8	0	0
PWE	6	1	1	0

S26. Would a weekly replacement be adequate?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	1	4	7	3
PWE	3	5	0	0

S27. Would a bi-weekly replacement be adequate?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	5	6	4	0
PWE	2	4	2	0

Wearer interface

S28. Should give instant feedback to you before a seizure?

	Strongly agree	Agree	Disagree	Strongly Disagree

CG	8	7	0	0
PWE	4	3	1	0

S29. Should give instant feedback before automated intervention?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	7	7	1	0
PWE	3	5	0	0

S30. Should only monitor the risk of SUDEP?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	0	5	7	2
PWE	0	4	4	0

S31. Should send alerts to the user?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	7	6	2	0
PWE	4	3	1	0

S32. Should send alerts to emergency units?

	Strongly agree	Agree	Disagree	Strongly Disagree

CG	6	6	2	1
PWE	3	4	1	0

S33. Should send alerts to caregivers?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	12	3	0	0
PWE	3	4	0	1

S34. Should a specific alert be sent to the caregivers in case the device is wrongly removed?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	14	1	0	0
PWE	5	2	1	0

S35. Should a specific alert be sent to the medical team in case the device is wrongly removed?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	4	6	4	1
PWE	2	4	2	0

How would you prefer to interface with the device?

S36. Small green light when active, red light when inactive on the device itself?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	10	4	0	0
PWE	3	3	0	2

S37. An app-notification on your phone interface for turning on, stand-by, connecting, notification for active device, notification if the measurement is on-going?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	10	5	0	0
PWE	4	3	0	1

S38. Would a non-flashing light for battery replacement be a good addition?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	7	5	2	0
PWE	3	5	0	0

Clinical Accuracy

Imagine the device is 100% reliable

S39. Would you expect the device to automatically promote an intervention (i.e., administer a drug)?

	Strongly agree	Agree	Disagree	Strongly Disagree

CG	5	8	2	0
PWE	5	3	0	0

S40. Would you accept an automatic intervention, but only when the device recorded dangerous levels of a SUDEP Biomarker?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	3	10	0	1

S41. Would you expect the device to inform the user if an intervention has been made?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	8	6	1	0
PWE	7	1	0	0

S42. Should the device inform the user of vital signs at the end of the seizure (i.e. stabilization of vital signs, SpO2, ECG parameters)?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	10	4	1	0
PWE	8	0	0	0

S43. Should provide you track record of SUDEP risk?

	Strongly agree	Agree	Disagree	Strongly Disagree

CG	8	7	0	0
PWE	6	2	0	0

S44. Would you expect the device to reduce your trips to hospital, or emergency services?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	5	9	1	0
PWE	4	3	1	0

S45. Would you like for your medical team to have access to the information as part your care?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	8	7	0	0
PWE	4	4	0	0

S46. Could work alongside your medical care team, instead of replacing them?

	Strongly agree	Agree	Disagree	Strongly Disagree
CG	7	8	0	0
PWE	5	3	0	0

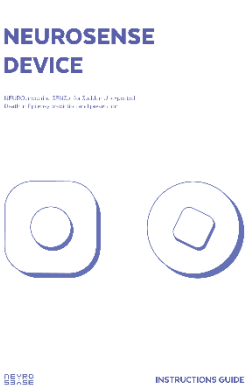
Appendix S4 – Materials used in the Workshop Insights into Action

Fig. 1- Exterior and interior of the kit with the materials used in the workshop.

Fig. 2- Instruction book in use.

Fig. 3- Stickers and cards with questions developed for the workshop.

Fig. 4- Device models.



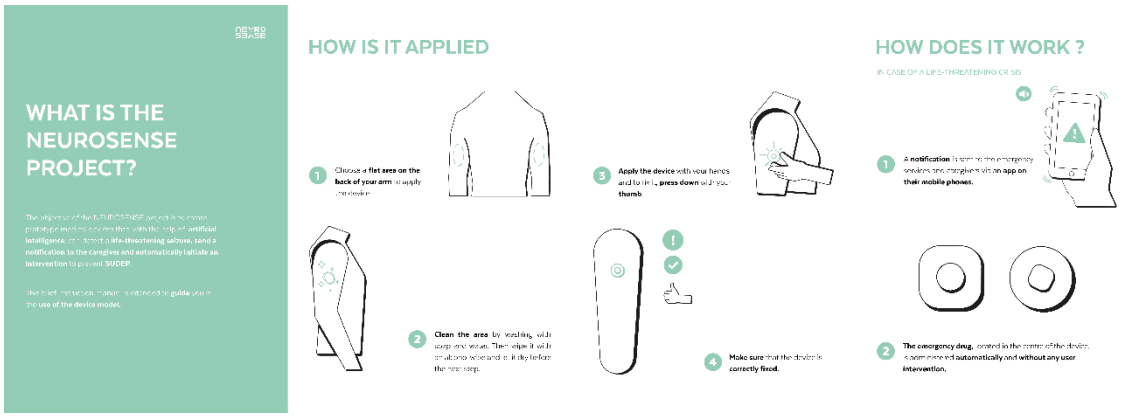


Fig. 5- Instruction booklet on how to use the models.

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