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Brain-computer interfaces: barriers and opportunities to widespread clinical adoption

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Dedication

To all the people that have been part of my life in some way.

To family, those ones who have been there from the beginning, have always been there and will always remain there, by my side.

To friends: the old ones, the new ones, the close ones, the close ones that are not physically close, all and one each single of them.

To people that have somewhat crossed into me and my life.

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Resumo

As interfaces cérebro-computador (BCI) são uma Neurotecnologia emergente com potencial para serem aplicadas no âmbito clínico, nomeadamente em condições de foro neurológico. Existe um interesse crescente no uso desta tecnologia para ir de encontro às necessidades clínicas de doentes com poucas soluções de tratamento e apoio médico.

Apesar das potencialidades das BCI para serem usadas em contexto clínico em humanos, as suas aplicações têm-se limitado a contextos específicos de pesquisa e sem transição para a área da saúde com consequente adoção enquanto ferramenta terapêutica.

Com este trabalho pretende-se rever as aplicações clínicas atuais destes dispositivos em humanos, perceber quais as barreiras e oportunidades para a sua adoção em contextos clínicos e retirar ilações do uso de BCI para políticas de saúde e gestão de inovação na prática médica.

A metodologia foi dividida em duas fases, que incluíram uma revisão sistemática das potenciais aplicações clínicas de BCI e um estudo qualitativo, usando *focus groups*, para melhor perceber e integrar as experiências, perceções, ideias e sentimentos de profissionais em relação à adoção de BCI na prática clínica comum. Os *focus groups* incluíram profissionais das áreas médica, de engenharia e de gestão.

As aplicações clínicas com maior nível de evidência para a clínica incluem a neuroreabilitação com BCI não-invasivos e o controlo de dispositivos de assistência com BCI invasivos.

Atualmente, diversas barreiras à implementação de BCI em contexto clínico, incluindo o desenvolvimento tecnológico, parecem ser possíveis de ultrapassar num prazo razoável. Contudo, barreiras sistemáticas à inovação e intervenções tecnológicas no âmbito dos sistemas de saúde, apresentam-se como um problema mais complexo e necessitarão de uma abordagem mais globalizada e multidisciplinar para tornar possível a adoção de BCI na prática clínica.

Para atingir este objetivo e ultrapassar estas barreiras, profissionais das áreas de medicina, engenharia e gestão devem colaborar e trabalhar em conjunto em contextos

de saúde, contribuindo para uma mudança de cultura e tornando os sistemas de saúde mais abertos à inovação.

Palavras-chave

Interfaces Cérebro-Computador;Interfaces Cérebro-Máquina;Neurotecnologia; Dispositivos médicos;Inovação em Saúde

Abstract

Brain-computer Interface (BCI) is an emerging neurotechnology with potential applications involving primarily neurological disorders. There is a rising interest in the use of BCI to address current unmet clinical needs from patients.

Despite their therapeutic potential, BCI use is still mostly limited to research stages and its translation into mainstream clinical applications and widespread adoption is lagging.

This study revises the current potential clinical applications of BCIs in humans, attempts to understand barriers and opportunities to wider clinical adoption and draws health policy and management implications of BCIs use in medical practice.

The methodology followed a two-step approach which included a systematic review of potential clinical applications of BCIs and a qualitative study, using focus group method, to understand and integrate professionals' experiences, perceptions, thoughts and feelings on the wide clinical adoption of BCIs. Focus groups included professionals from the medical, engineering and management field.

BCI clinical applications with more clinical evidence include neurorehabilitation with non-invasive devices and the control of assistive devices with invasive BCIs.

Nowadays, several barriers to wider clinical adoption of BCIs, including technological, seem addressable. However, systemic barriers from the health systems to innovation and technological interventions need a comprehensive and multidisciplinary approach to enhance their adoption.

Professionals from medicine, engineering and management, working in collaboration in healthcare contexts, are some of the stakeholders important to change the current vision of healthcare towards innovation.

Keywords

Brain-Computer Interfaces;Brain-Machine Interfaces;Neurotechnology;Medical devices;Health Innovation.

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List of Acronyms

AAC	Augmentative and Alternative Communication
ADHD	Attention Deficit Hyperactivity Disorder
ADL	Activities of daily living
AI	Artificial Intelligence
ALS	Amyotrophic lateral sclerosis
BCI(s)	Brain-Computer Interface(s)
COREQ	Consolidated criteria for reporting qualitative research
CNS	Central nervous system
DBS	Deep Brain Stimulation
DOC	Disorders of consciousness
EEG	Electroencephalogram
EU	European Union
FDA	Food and Drug Administration
FES	Functional electrical stimulation
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HTA(s)	Health Technology Assessment(s)
IP	Intellectual property
LIS	Locked-in Syndrome
MCDA	Multicriteria decision analysis
MDR	Medical Devices Regulation
MeSH	Medical subject heading
N/A	Not applicable
NIH	National Institutes of Health
QoL	Quality of life
R&D	Research and Development
SD	Standard deviation
SCI(s)	Spinal cord injury(ies)
TALC	Technology adoption lifecycle
TBI	Traumatic brain injury
UBI	Universidade da Beira Interior
USA	United States of America
WEF	World Economic Forum

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1. Introduction

Illness or injury that results in damage to the brain and its functions can lead to serious dysfunction and disability since, although new functional connections may be formed, the brain has a limited capacity to repair damaged tissue(1).

High global incidence of many serious neurological and mental health disorders generate considerable economic burden, not only through direct health care costs but also in lost productivity(1,10). There is a paucity of effective treatments for some these disorders which means the accumulation of many unmet health and healthcare needs.

Innovative approaches that counteract the varied impacts of these diseases on social, economic and everyday life of patients and their families are needed play(3). Novel neurotechnologies offer potential routes to meeting some of these needs, but pathways to mainstream innovative and effective treatments are still a challenge.

Brain-computer Interface (BCI) is an emerging neurotechnology, that is defined as "a communication system in which messages or commands that an individual sends to the external world do not pass through the brain's normal output pathways of peripheral nerves and muscles", providing "an alternative method for acting on the world"(4). In short, BCI technology provides direct communication between the brain and an external device, which can assist with numerous diseases(3). A more detailed definition of BCI is in section 2.1.1. "BCI".

Clinical interest on BCIs is driven by the increasing number of people requiring rehabilitation following problems such as stroke (increasing populational ageing), and the global phenomenon of insufficient numbers of therapists able to deliver rehabilitation exercises to patients(5).

Potential applications might involve pathology due to stroke, degenerative diseases, developmental disorders, and other acquired disorders. Targeted functions could include motor, cognitive, emotional, and perceptual disorders(6,7).

In principle, BCIs may assist users to communicate, control prostheses or wheelchairs, support rehabilitation, making these technologies potentially useful for therapeutic uses and help to address current unmet medical needs (1), therefore they might be significant to help managing, and in the future even treating, this conditions, as they play an efficient and natural role in the attempt to provide assistance and preventive care to people with neurological disorders(3).

Although BCIs have demonstrated a potential use in clinical settings, and even independent home use by patients, the use of this devices is still confined to research contexts(1,5,6).

Currently, BCIs are recognized as a technology with potential to influence the future of healthcare and medicine and have been gaining spotlight, raising more investment to

research(10). Nonetheless, large and mainstream clinical adoption is lagging as several challenges need to be addressed.

1.1. Current challenges

At present, BCI research and development remain for the most part confined to the laboratory and studies involving real patients often remain small clinical trials closely overseen by the researchers(8,9). The translation of these devices from laboratory progress to clinical use and wide clinical adoption, contributing to improve the daily lives of patients, is in its initial stages(8,9).

Several factors contribute to the gap between the proof-of-concept or small clinical trial stages to generalized use of BCI in clinical contexts. The more disruptive a new technology is, the bigger this gap between its conceptualization and its adoption into healthcare systems(13).

When evaluating the use of these devices and its readiness to clinical use, some risks should be considered along with unintended consequences of BCIs. Invasive BCIs, beyond carrying the risks associated with neurosurgery, may cause local neural and vascular damage and increase the risk of infection(1). This damage can also interfere with the technological components itself, interfering with its reliability(1). Regarding non-invasive BCIs they are not so efficient and its performance may be affected by fatigue and distraction(1).

Technical challenges are also of major importance. These are related to materials, electrodes and sensors, signal recording and computation, signal processing, modelling and control, communications and robustness(14). Safety and reliability of the device and its components is key as well as security and usability(14).

As BCIs integrate multiple technologies, that might be in a different stage of readiness, development of standards to ensure they comply with defined criteria of safety and effectiveness may ensure stakeholders trust in these devices(15). However it is important to balance this need for standards with the acknowledgment that some of these options are at an emerging developmental stage and not mature enough to be standardized(15).

Besides BCIs own technological barriers, engineers, scientists and device developers struggle to navigate funding, pass regulatory reviews, reimbursement process, making harder to establish a sustainable marketplace(12).

In the healthcare sector, innovations like BCIs have the potential to improve some patients' Quality of Life (QoL), but they also offer a challenge to existing providers and systems to its adoption. Most innovations in healthcare are incremental and disruptive innovations are rare(16). The more disruptive a new technology is, the bigger the gap between its conceptualization and its adoption into healthcare systems(13) and these technologies often face hurdles in their commercialization that impact its clinical adoption(17).

Neurological devices development have been dependent on its early stages from public financing and research grants that provide sufficient support to basic and foundational work that underlies the initial hypothesis-building phase of development(12). However this investment fail to provide a continuous platform for the sustained research that includes various development stages required to achieve scalability, demonstrate commercialization and adoption strategies, initiate verification and validation and all the steps needed for this devices to enter the healthcare system(1,11).

In fact, funding has a key role in the field. Public investments have focused on early research phases, rewarding the novelty and more eye-catching results, leaving the technologies underdeveloped, inaccessible to patients and without the funds to a continuous incrementation that may evolve in more concrete clinical applications with the potential to a widespread benefit(1,11).

Beyond the acknowledge importance of Neuroethics, it is also determinant to consider society perspectives on the use of this technologies. Technological advancements may affect stereotypes in society and it is major to investigate how this development will affect psychological processes but also perceptions and interactions in the real world(18). Society perceptions will have influence on adoption, but at the end we must remember patient will choose and that autonomy is to be respected.

Neurotechnology is a complex field and that calls for a more comprehensive and multidisciplinary approach both to its development and to its adoption(2). Not only there is the need for boundary spanning between Health and Engineering, but also to involve Social and Behavioural Sciences, as well as patients and caregivers, throughout all the R&D process. The discussion of a clear path, which consider guidelines and agreed standards, towards translation of BCIs to clinical practice, which includes all stakeholders and improves collaboration, may enable a better adoption in the healthcare systems when these devices reach the appropriate maturity level for large-scale adoption.

1.2. Aim

The aim of this study is to understand the barriers to wider clinical adoption of BCIs in medical practice. This aim can be broken down into three sub-objectives:

1. Describing the current potential clinical applications of BCIs in humans and to what patients.

2. Understanding barriers and opportunities to wider clinical adoption of BCIs.

3. To draw health policy and management implications of BCIs use in medical practice.

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2. Background

Research in the field of BCIs has historically generated high and many premature announcements of clinical success based on single case studies or uncontrolled observations, contributing to discredit the field early on(19). This may have contributed to halted funding from public sources and block of large controlled clinical studies, despite some indications of its efficiency(19).

In the last two decades there has been a concerted effort by groups of clinicians, neuroscientists and engineers to properly research BCI systems, integrating robotic systems with brain signals correlated with a patient trying to actively generate a movement, or imagine a motor action, to enhance and recover lost functions(5). This effort coincided with the early 2000's BrainGate research program as one of the big hopes for the development of this devices(20).

BCI research continues to grow at a rapid rate, as evidenced by the number of peer-reviewed publications in this field over the past 20 years (Figure 1), but more than 20 years later after the first studies of BCIs in humans the use this neurotechnology as a clinical treatment for some brain disorders continues not to meet expectations(21). BCI didn't live to the initial hype and clinical research is still far from being accessible to everyone in need and who can benefit from it.

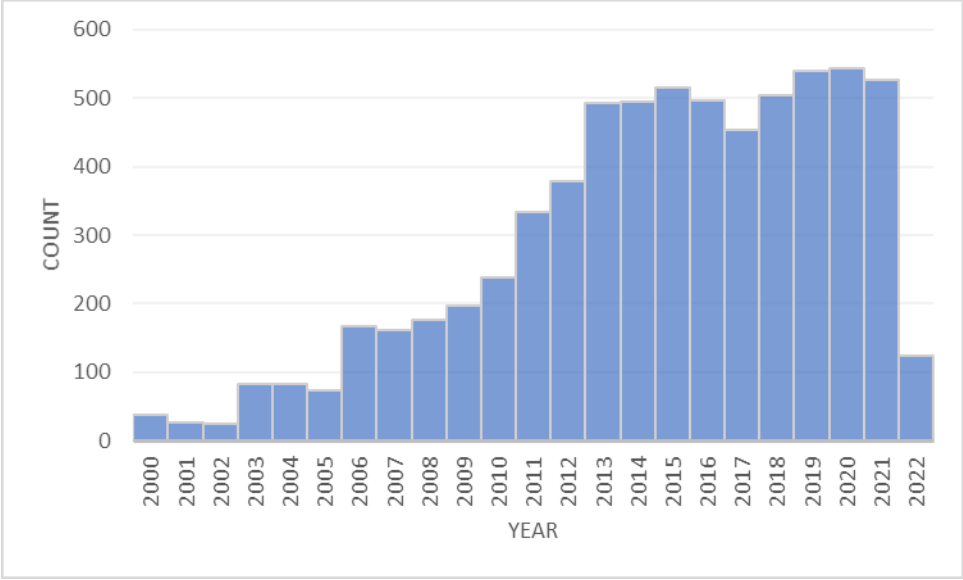


FIGURE 1 | Articles with keywork "Brain-computer interface" in peer-reviewed literature, from 2000-present (source: PubMed)

Numerous ground-breaking advances in sensors and computational tools herald great promise for more sophisticated and user friendly BCI systems requiring no or little maintenance(22).

In addition to hi-fidelity signal acquisition, significant progress in signal processing and machine learning tools, high computation power and increased wireless solutions have

significantly contributed to BCIs(22). The future of BCI will on elucidating the underlying psychophysiological and neurological factors that potentially influence BCI performance(22). Challenges are inherent in translating any new technology to practical and useful clinical applications, and BCIs are no exception(11). Even when all current challenges are met, BCIs will still face healthcare systematic challenges to wide clinical adoption of technology.

While BCIs adoption seems to be hindering in clinical contexts, direct-to-consumer BCIs seem to be in a new phase of hype (Annex 1) as an extended reality technology(23). One direct-to-consumer application of BCI technology that may have impact in healthcare is wellness ad consumers will use BCI trying to improve physical, mental, and social well-being(24,25).

In this context, it is important to remember wellness and medical fields have major differences. Usually medical neurotechnologies are regulated, subject to approval an oversight, by appropriate administrative bodies, although due to BCIs still exploratory phase it may be used outside traditional clinical instances, mainly for research(26). On the other hand, wellness acts on an "off label" and/or "grey" area, without making medically recognized diagnostic or therapeutic claims, and as such are not regulated by the same mechanism as medical neurotechnologies(24).

2.1. Working definitions

2.1.1. BCI

A BCI is a system that acquires brain signals, analyses and translates them into computerized commands that then are relayed to an output device to carry out a desired action by the control of external devices, such as communication devices, functional electrical stimulation (FES), or exoskeleton robots, among others (Figure 2)(3,4,6,11,28). The BCI system may also include a feedback stimulus for better sensorimotor integration(29,30). This feedback mechanism may come from external stimulus or by indirect input to brain cells(29–32).

Although its denomination just references the interaction and interface between a brain and a computer, an overlap between terms may occur. In the context of this work, we draw a distinction and the term BCI will be used just for the case where brain signals are used to bring about an effect in the outside world. Therefore, the term BCI involves an outward translation of signal from the brain(1).

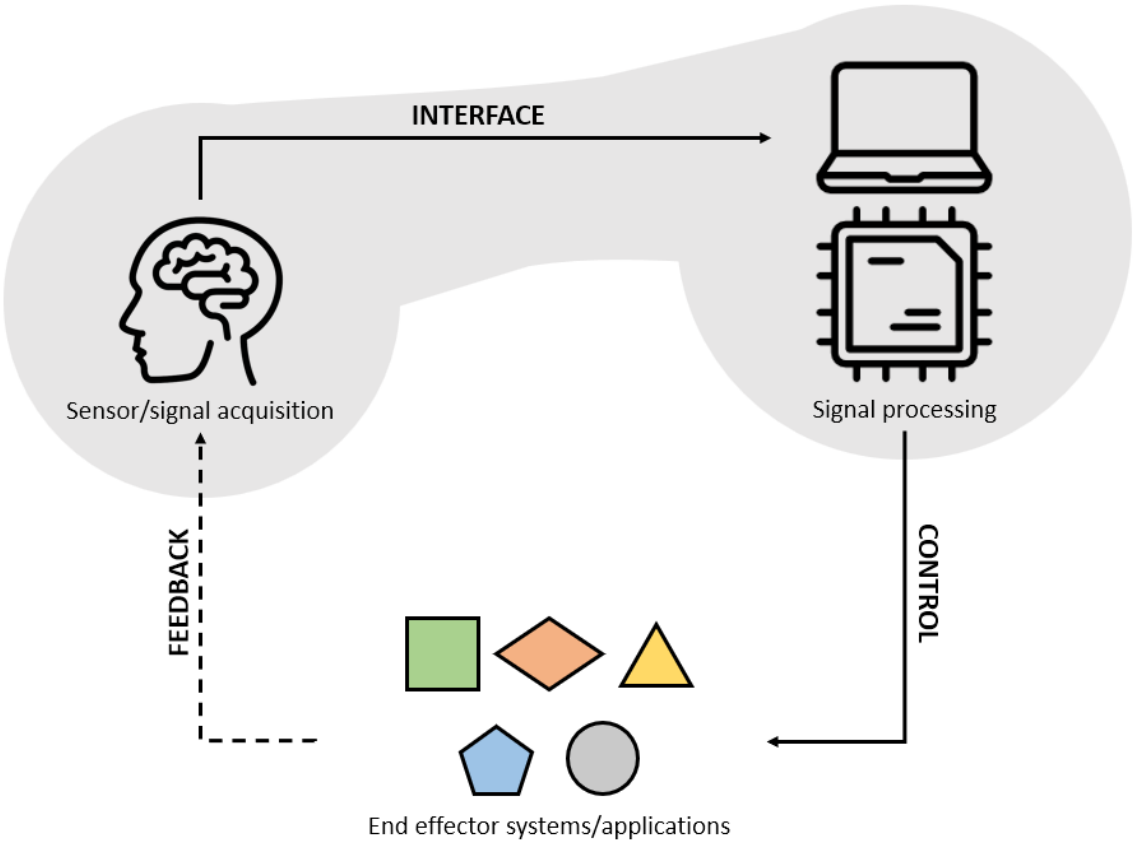


FIGURE 2 | A BCI system

To acquire brain activity signals, either invasive or non-invasive strategies can be used(27). This work will not differentiate minimally invasive procedures to implant BCIs. Invasive BCIs will be the term used when some type of surgical procedure is needed to implant the device, and non-invasive BCIs will be considered BCIs that won't require surgical procedures to be used, as they are not implantable. Although this may seem a simple classification in terms of invasiveness, the aim of this work is not influenced by this classification.

Although BCI research has used a variety of brain signals to provide communication and control options(6), a detailed distinction or classification based on signals acquisition mechanisms will be studied as this is outside the scope of this thesis.

Regarding its end application, research has mostly been divided in two approaches: assistive BCIs aiming to bypass the damaged neuronal pathways by providing a continuous and permanent alternative for communication and control of external devices(33); and rehabilitative BCIs aiming for the recovery of damaged neuronal links and thereby the restoration of impaired functional capabilities by effective facilitation of neuro-plasticity(33).

2.1.2. Health Innovation and wide clinical adoption

Innovation, in general, can be defined as a process that starts with an invention, goes through an adoption process and ends in wide diffusion(34). In healthcare, successful innovations bring

clear benefits when compared to what is currently done, and often possess two key qualities: they are both usable and desirable(34).

New clinical technologies have the potential to bring important benefits to health care however, achieving an optimal spread of new clinical technologies into health care has proved to be far from straightforward(35).

Successful implementation of technology depends on negotiating the changes this requires to staff activities and adapting implementation to the wider organisational and social context(35).

The process that takes place when adopting a new technology to clinical settings can be regarded as comprising three main stages: initiation, the adoption decision and implementation(35). Wide clinical adoption would be a circular process comprising all these stages, leading to a routine use of the adopted technology.

Table 1 provides an overview on what may be considered a BCI wide adopted in clinical settings when compared to a BCI in research phase. This table is based on two general publications for scaling up health innovations and one on digital innovation in healthcare(36–38). To consider that a BCI has achieved wide clinical adoption, it will need to comprise all the topics referred in this table.

TABLE 1 | Wide clinical adoption of BCI compared to research phase BCI

	Research phase	**Wide clinical adoption**
Device regulation	Device not yet approved by regulators	Use of an approved medical device
Clinical practice	Experimental surgical procedure (if applicable)	Mainstream surgical procedure (if applicable)
Clinical indication	Applicable to clinical contexts in research	Clear clinical indications
Reimbursement	No reimburse	Reimbursed is provided for the device
Integration in healthcare	No pathways defined	Implemented in clinical pathways
Access	Just available to some patients	Easy access for anyone who may benefit
Social acceptance	Society has reservations regarding the device	Widely accepted by society

2.2. Context

The association between breakthroughs in health, or advances in treatment of medical conditions, and discoveries related to drug development is still the main paradigm in clinical treatment(2).

Adoption decisions regarding interventional procedures and medical devices are more complex than for pharmaceuticals for a variety of reasons(35). These include the fact that outcomes often depend on operator skill, with a learning curve to be negotiated; health technology assessment (HTA) processes have only recently been established; additional physical infrastructure is often required; and good quality data on cost-effectiveness is often not available(35).

Besides these factors, medical devices have a relatively short product life cycle with variable prices and interventional procedures are generally delivered to a heterogeneous patient population(35).

This paradigm may delay the adoption of technologies, as healthcare practitioners will not be aware or confident using it. However, technological solutions are proving to be valuable and to address treatment to conditions usually seen as intractable(2,10).

Innovative healthcare technologies can include new models of care and ways of organising services, staff, care pathways and guidelines making changes to organisational systems needed when new devices or procedures are put in place(35).

2.2.1. Healthcare ecosystem

Regarding the healthcare ecosystem, this is a particularly complex system, as many actors or stakeholders influence or make decisions at various levels using systematic reviews, HTAs, guideline recommendations, coverage decisions, selection of medicines or diagnostics, quality improvement, and policy or evidence briefs(39).

This intrinsic complexity may lead to duplication of efforts, inadequate use of scarce time and resources and confusion and conflicts, if decisions are not well aligned or in the absence of broad coordination(39).

Key stakeholders and actors often comprise regulators, authors and organizations coordinating systematic reviews, HTA agencies, guideline developers, coverage decision makers, quality improvement actors and evidence-makers policy makers(39). All these actors are independent, but closing the gaps between disciplines and bridge new partnerships may result in solutions to overcome the fragmentation among the stakeholders leading to smoother implementations of new approaches(39).

In the context of novel neurotechnologies, policy makers need to think about the public benefits of science and technology-based research. Top priorities should include a clear identified need,

assurance of security and safety, robust evidence, continuous reflexive evaluation coordinated interdisciplinary action and effective and proportionate oversight(1).

Health Innovation should be justified in terms of its public benefits(1). In the case of BCIs this means meeting therapeutic need. It is imperative to resist the technological paradigm of pursuit the novelty and important to understand that products that are indistinguishable in terms of the benefits do not bring value to the patients(1).

Protecting safety is central to regulatory regimes governing medical technologies(1). Risks of using BCIs for clinical purposes can only adequately be assessed relative to their efficacy in delivering therapeutic benefits and the availability of alternative treatments (when they exist), which highlights the importance of assessing efficacy as part of the regulatory process(1).

There are both regulatory and methodological reasons why the development of BCIs might not produce the most transparent, robust or balanced body of evidence. These include ungeneralisable and dispersed data from small-scale studies, the influence of commercial interests, and methods that encourage the publication of positive, but not disappointing, findings(1). Alternative methods of linking and disseminating evidence are likely to be needed to address this.

One approach to involve considerations of multiple criteria and actors are multicriteria decision analysis (MCDA), varied methodology for assessing complex issues across disciplines with greater application in economics(39). In healthcare, MCDA is used primarily to addresses the costs and benefits of options available to decision makers and could include stakeholder input, leading eventually to conclusions that are made in form of recommendations or decisions, that may overlap(39).

Recommendations, in the health context, are broadly defined as an actionable statement for the best course of action, put forward by an authoritative body(39). This body draws conclusions about the strength of recommendation or type of decision, assessing the extent to which one can be confident that the desirable consequences of an intervention outweigh the undesirable ones(39). One example of this assessments is the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework, in which the recommendation can be strong or conditional and be issued for or against interventions or options(39).

Decisions differ from recommendations because decisions are binding in some form(39).

The development of neurotechnologies is unlikely to follow simple linear innovation trajectories. Reflecting and understand the directions in which research is travelling, can help to guard innovation against pathways that do not serve public benefit(1).

2.2.2. Challenges to innovative technologies

Innovation in healthcare and in the BCI field is often multidisciplinary. Coordination between different disciplines is needed to protect against potential risks posed by gaps in the collective understanding and oversight of a technology's risks and capabilities(1). Interdisciplinary collaboration also offers opportunities by introducing diverse visions of potentially fruitful development trajectories.

Tensions between needs and uncertainty that lies in the use of these devices presents a particular challenge to effective regulation and governance of BCIs(1). A proportionate approach to support innovation while protecting safety is needed and hard-law regulation will not always be the most suitable means of achieving this(1).

Surveillance mechanisms for the use of BCIs should be robust and may be strengthened by making it mandatory for clinicians to report adverse events and by making all information on adverse incidents and incident accessible(1).

Uncertainty about the benefits, risks and mechanisms by which BCIs achieve their effects presents one of the central ethical challenges in clinical wide spread adoption(1). Regulation of medical devices does not itself encourage collection of extensive clinical evidence, but collaborative efforts to improve information governance and data linkage by manufacturers, practitioners and others are needed(1).

Some approaches that may enable the wide clinical adoption of BCIs are already in place. Significant research efforts on a global scale have delivered common platforms for technology standardization and help tackle highly complex and non-linear brain dynamics and related feature extraction and classification challenges(22).

Both the Brain Research Through Advancing Innovative Neurotechnologies® (BRAIN) Initiative and Human Brain Project will help bringing together different players to better understand the brain and improve research in the field of brain disorders(40–42). On the technological side there are already initiatives that look for BCIs and how to better develop safety and usable systems(13,14). Several entities have also acknowledged the growing importance of Neuroethics. The creation of a Neuroethics framework, the NeuroRights Foundation and the discussion and development of recommendations on responsible innovation in Neurotechnology are examples of initiatives in this area(25,43,44).

From regulatory agencies, United States Food and Drug Administration (FDA) has also take some steps through the creation of a Breakthrough Devices Program and a guidance for Implanted BCI Devices for Patients with Paralysis or Amputation(45,46). However it is important to not forget there is a gap between regulatory approval and the commercial viability and clinical access of a device(12).

New technologies often face hurdles in their commercialization that impact its clinical adoption(17). This is even more truth with disruptive ones like the case of BCIs. Technology adoption lifecycle (TALC) and its implication in the translation of this devices (Annex 2) is very important for the industry and should be regarded in aggregation with issues like the clinical necessity, scientific validity, technologic maturity, deployment cost, workflow viability and economic viability(17). TALC is a diffusion of innovation through time that proceeds from innovators and early adopters into the population majority and illustrates the chasm between technology adoption from pilot research to mainstream clinical practice(17).

This can be correlated this with the "research-to-industry valley of death" (Annex 3). This represents a gap between the public investment from Government and Universities in basic technology research and the major investment from private sector in the development of more mature technologies(12). This gap may lead to the "death" of a technology, hence the metaphoric name, with "academic maturity" but without funder for financing the follow-up stages(12,13).

The need to invest more into innovation management that encompasses the entire spectrum from the ideas, Research and Development (R&D) process through its adoption as a new standard of care(16). One major factor is to listen and integrate all the stakeholders, diverse backgrounds and cultures and the healthcare system itself in the process.

Neurological devices development have been dependent on its early stages from public financing and research grants that provide sufficient support to basic and foundational work that underlies the initial hypothesis-building phase of development(12). However this investment fail to provide a continuous platform for the sustained research that includes various development stages required to achieve scalability, demonstrate commercialization and adoption strategies, initiate verification and validation and all the steps needed for this devices to enter the healthcare system(1,11).

Nowadays some public organisms, like the National Institutes of Health (NIH), are already making some changes in funding mechanisms, providing specific funding through programs aiming to develop, demonstrate and disseminate scientific and operational innovations, which improve the efficiency and effectiveness of clinical translation from identification to first-in-human studies to medical practice implementation to community health dissemination(47).

In the future, neurotechnology devices as BCIs, have the potential to provide viable solutions in areas where pharmaceutical treatments don't exist or have low positive results(14). We may be in an inflection point, with more interest in the BCIs market and more will and money to invest in this market. It is important to start the discussion on the clinical use and large-scale adoption early, without kill the potential advances in the field and remain openminded to new contributions. This is still an emergent field but start paving the way before scale-up and integration in the Healthcare Systems and clinical practice may enable a better and more comprehensive adoption of BCIs.

3. Methodology

The methodology followed a two-step approach. First, a systematic review on the potential clinical applications of BCIs in humans and later a qualitative study, using focus group method to understand and integrate professionals' experiences, perceptions, thoughts and feelings on the wide clinical adoption of BCIs. Appendix 1 includes the timeline of the research conducted.

3.1 Systematic review

The systematic review occurred from August 2021 and its protocol was registered on September 13, 2021, on the International Prospective Register of Systematic Reviews (PROSPERO) and details can be accessed at https://www.crd.york.ac.uk/prospero/ (ID: CRD42021273207). At the time this work, this systematic review is still unpublished.

Records included in databases were searched and identified from 2015 to September 1, 2021. References were searched in PubMed, Embase and Cochrane Library. The search strategy and terms and selection criteria were based on the PICO system (Table 2) and developed for PubMed and then applied to the other databases. Due to the exploratory format of this review and to get a better look and understanding of the current applications of BCIs with clinical potential, there were no restrictions on study design, so all designs were accepted. Due to this choice, it is important to note that reviews or books may contain results from studies previous to 2015.

TABLE 2 | PICO parameters

Population	Patients using BCIs
Intervention	BCIs
Comparison	Standard treatment or no comparison
Outcome	Relevant clinical applications of BCIs

Terms used for the search were: "brain-machine interface" OR "brain-computer interface" AND clinical OR medical (Table 3). The databases were checked for predefined medical subject heading (MeSH) terms, which were then integrated in the research strategy.

TABLE 3 | Keyword combination

Set 1 (OR)		**Set 2(OR)**
Brain-computer interface	AND	Clinical
Brain-machine interface		Medical

Paper selection process included four stages: first, the identification of studies according to the search parameters; second, the application of a filter using the eligibility criteria; third, a screening phase, which filtered the studies, eliminating those that did not fit the research approach according to the inclusion and exclusion criteria in Table 4, and/or those that appear in multiple databases; and finally, an inclusion phase, which allowed the identification of relevant studies to be included in the review.

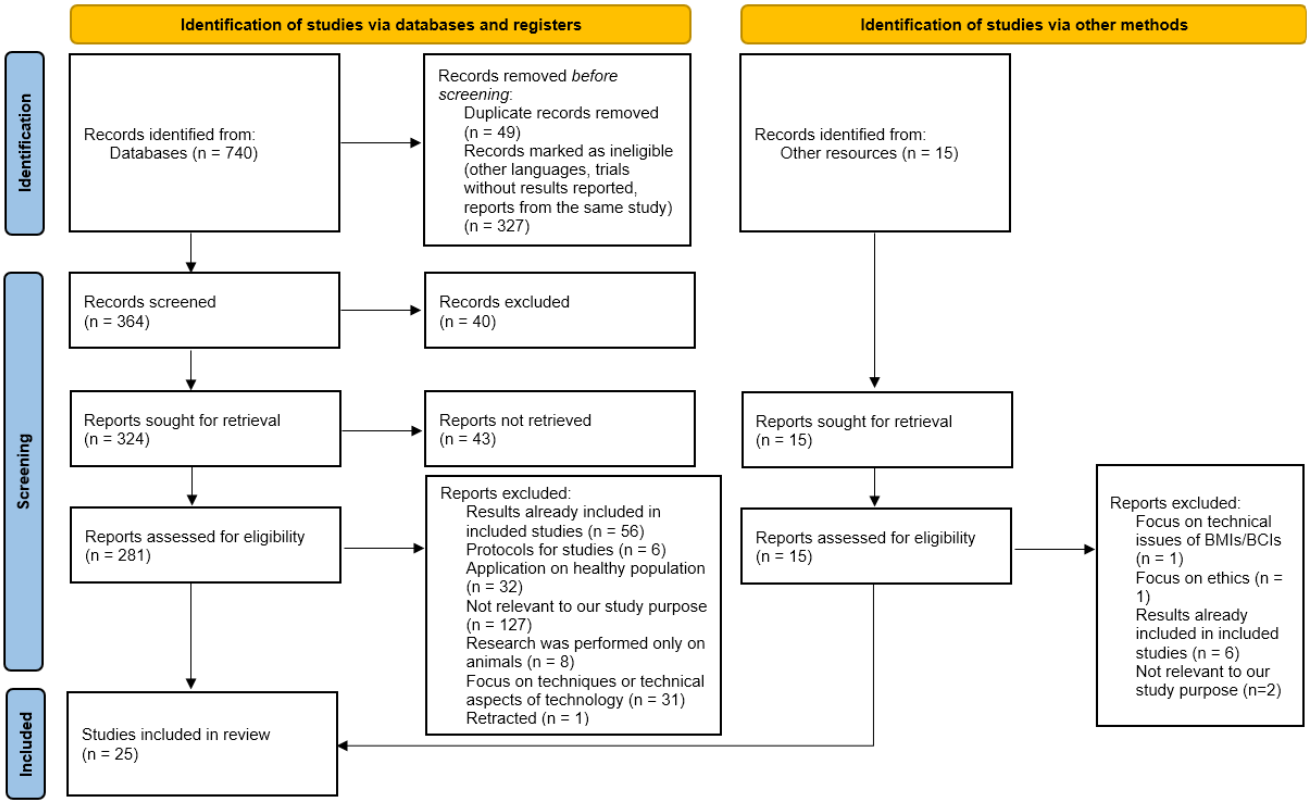
TABLE 4 | Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Scientific publications in English or Portuguese	Scientific articles in other languages
Involving adult humans with clinical conditions	Involving animals, healthy subjects or children (age <18 years old)
From 2015 to September 1, 2021	BCIs used as assessment tools or biomarkers without treatment
	Aim of the study was to investigate basic mechanisms only
	Protocols
	Not fit to the inclusion criteria

After, titles and abstracts to identify potentially relevant records were reviewed. Final eligibility assessment of potentially relevant articles involved examining the full texts.

To ensure that all possible articles relevant for the systematic review had been included, the process was completed by searching the references of the studies initially included. No records were exclude based on study type, outcomes, or number of participants. As all types of designs were included in this work, results reported in more than one study were eliminated. This was the case where some reviews and systematic reviews had already described and analysed smaller studies.

A total of 740 records were identified from the database search and 15 additional references were included in assessment and the selection process as described at Figure 3. A total of 25 studies, published from 2017 to 2021, were included in the review (see Appendix 2 for more information regarding the included studies).



Adapted from Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. (2020)(79)

FIGURE 3 | PRISMA Flow Diagram

Results were described and synthetized in a narrative way. Ideas from the literature review analysis were mapped against topics, developed by The World Economic Forum (WEF) on technology and Health. The diagram and respective dynamic briefing created allowed a general comprehension of common subjects on BCI, technologies, health and society (Annex 4).

The AMSTAR 2 tool checklist(48) for a critical appraisal of systematic reviews that include randomised and non-randomised studies of healthcare interventions is available at Appendix 2.

3.1.1. Risk of bias

As this is an emerging field the sample sizes of some studies may not be adequate. This review may also have selective reporting bias as positive results are more likely to get submitted and published. Some of the studies may also be subjected to an observation bias as they will come mainly from publishers in medicine and technology areas.

3.2 Focus group

After reviewing the potential clinical uses of BCIs, focus groups were conducted to understand and integrate professionals' experiences, perceptions, thoughts and feelings on the wide clinical adoption of BCIs.

Focus groups are semi-structured discussions with a predetermined group of people that may be used to explore views on health issues, programs, interventions and research, exploring a specific set of issues(49). Therefore, focus groups are a data collection method with a small group of people to discuss a given topic, guided by a moderator using a questioning route(50).

The option for qualitative research, in the form of focus groups, is justified by the need to integrate what is already available in literature with the experiences, perceptions, thoughts and feelings of professionals working on the field of BCIs or with potential to be an agent on the widespread of these devices(51)(50). In this context, focus groups contribute to understand real-world evidence and compare it to what is described in the literature.

3.2.1 Study population

Target population were professionals with a medical or engineering background with, at least, basic knowledge about BCIs or neurotechnology. The medical professionals selected must had a specialty of Neurology, Neurosurgery or Physiatry as we selected these as the most important specialties for the BCIs field.

Representatives from the BCIs and neurotechnology area (Industry, Research Centres and academia, Companies) who may have a mixed background (engineering and management or healthcare and management) were also targeted as participants. Inclusion and exclusion criteria are described in Table 5.

TABLE 5 | Participant selection inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Have a medical degree with specialty of Neurology, Neurosurgery or Physiatry OR	No knowledge of our field of interest
Have an engineering degree OR	Neither a medical nor engineering professional
Be a representative or have a direction role linked to Neurotechnology stakeholders (Industry, Research Centres and academia, Companies)	Not fit the inclusion criteria
AND Have knowledge of the BCIs and neurotechnology field	

3.2.1.1. Sample

Participants were selected using a purposive sampling, therefore selection was based on judgment about which potential participants might be more informative(50).

Using the inclusion and exclusion criteria presented before, 102 potential participants were identified and emailed for recruitment to participate in this study.

Participants emails were obtained using public sources. These included published literature in which the invited participant was author, public pages of institutions where emails were available and social network (LinkedIn) with email publicly available.

All the potential participants were invited firstly by email. In the email was stated the focus group goals and expectations as well as the planned day for it to occur, to allow participants to plan their participation. Inviting emails were started to be sent in February 2022.

In the first emails, participants were also invited for a preliminary interview, in an informal context, to better understand the fields and expectations. This approach also allowed people that were interested in participating but did not have the time to be present at the focus group, to express their opinion and contribute to the introduction of some new ideas directly into the focus group discussion. A total of 10 preliminary interviews were conducted. Its content was not used for any results and will remain undisclosed and undiscussed.

After the first contact by email, and in the case of no reply, a follow up email or LinkedIn message (for cases where guests had a public and active profile) was sent, to access guests' availability and willingness to participate in the focus group.

For the participants who accepted to participate in the focus groups, an email explaining how the focus group would work and a consent to be signed by the participant was sent and an approval from Universidade da Beira Interior (UBI) Ethics Committee was obtained (Annex 5).

From the 102 invites sent, 55 answers were obtained. Of these, 18 were negative to our participation request. Of the remaining 37 guests: 22 participated in the focus groups, 9 were not able to participate due to scheduling incompatibilities and 6 were lost to follow up. A flowchart of this recruitment process is presented in Figure 4.

Distribution of participants by the three focus groups was made to allow multidisciplinary perspectives and according to participants schedule preferences. Participants with different background (Medicine, Engineering, representative from neurotechnology area), were integrated as shown in Figure 5, so at least one representative from the three main areas we considered was present in each focus group.

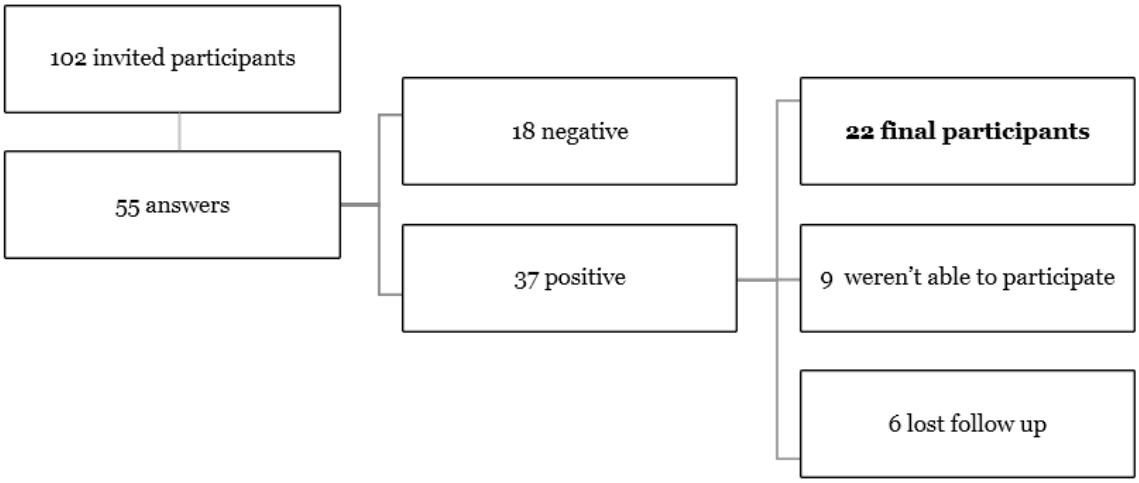


FIGURE 4 | Flowchart of participants' recruitment process

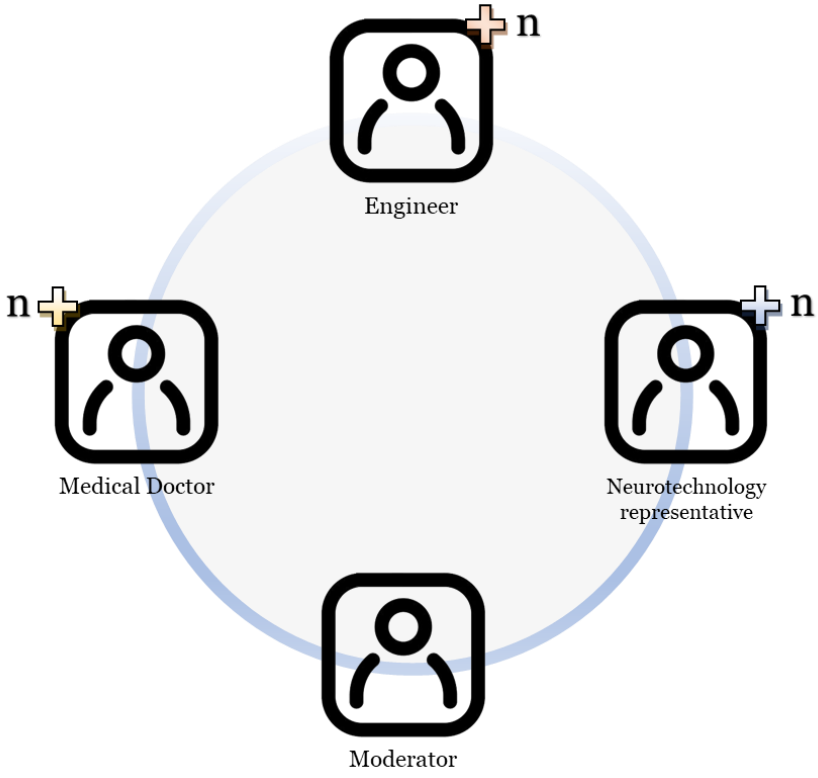


FIGURE 5 | Focus group ideal constitution

Regarding the composition of each focus group, we were able to have at least one representative from the three fundamental areas we considered (Medicine, Engineering, representative from neurotechnology area, as previously discussed and presented in Figure 5) in two of three focus groups, but in one of them we did not have a representative for the Medicine area. In this case, the moderator introduced some ideas from the previous focus group and preliminary interviews with participants from this area.

Demographic data from the participants was collected from public sources. Here is presented the background (Figure 6) and current based country at the time of the study (Figure 7) of the 22 participants.

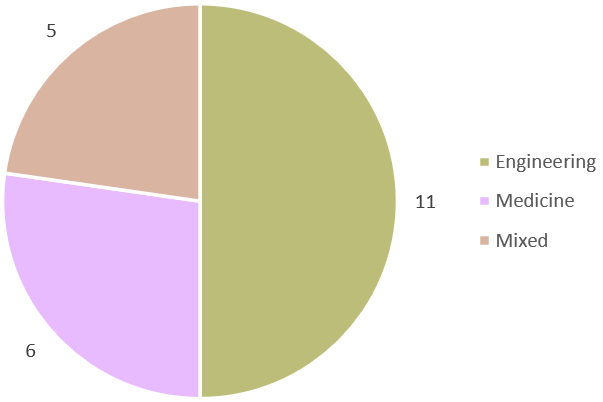
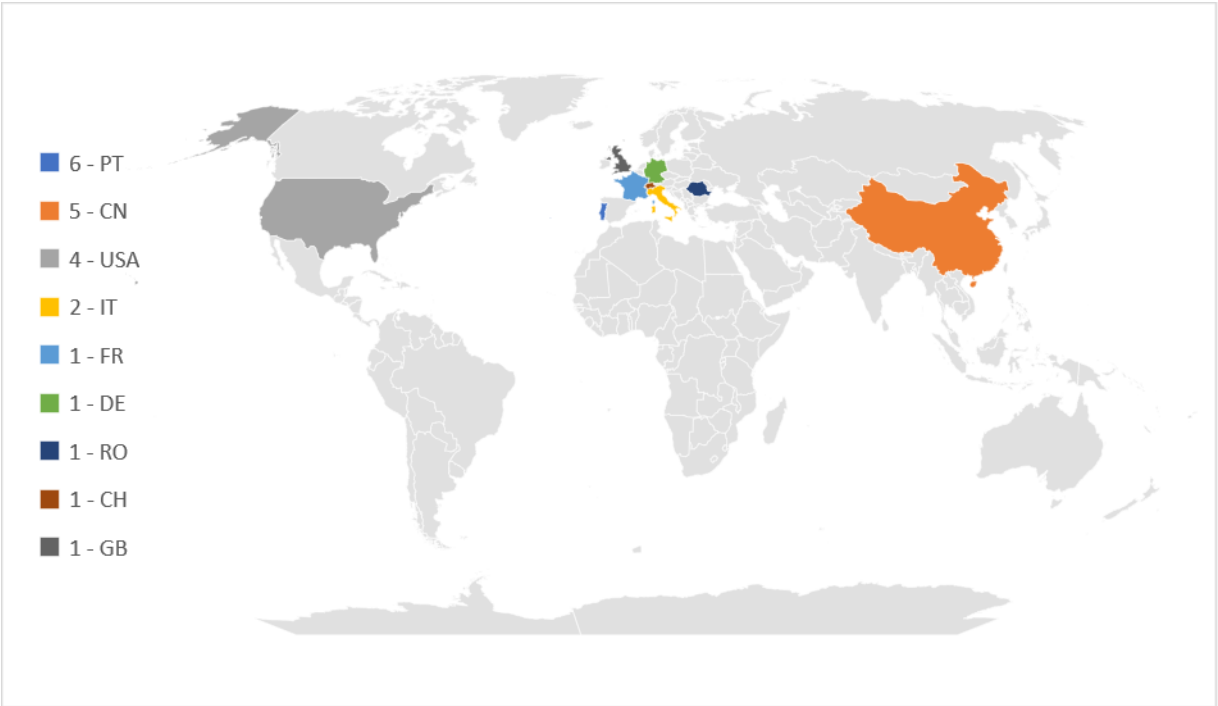


FIGURE 6 | Background of the participants (n=22)



(Labels, according to ISO country codes:
CH – Switzerland CN – China DE – Germany
GB – United Kingdom IT – Italy FR – France
PT – Portugal RO – Romania USA – United States of America)

FIGURE 7 | Current based country of participants at the time of the study (n=22)

3.2.2. Details of focus group meetings

Focus groups were programmed to last for a maximum of two hours, and they occurred online on a Zoom Meeting (using Zoom platform software, version 5.9.7 (3931) on a licensed account).

A Polls tool present in the Zoom platform was used to create polls to enable a more dynamic approach and get a quantitative view of the participants opinion. The questions were previously inserted in the platform and served as a catalyst to initiate the debate, to improve interaction and give us some quantitative preview.

The answers to the questions consisted of a 5-point Likert scale from strongly disagree to strongly agree (1-strongly disagree, 2-disagree, 3-neutral, 4-agree, 5-strongly agree). These questions in the form of poll are in Table 6 along with the topics suggested by the moderator, during the focus group.

TABLE 6 | Polls' questions and suggested topics from the moderator

Statement	Suggested topics to discuss
1. BCIs have the potential to be a solution for some current unmet clinical needs.	- General thoughts and perspectives - BCIs may bring value for some patients but more studies, research and development is still needed?
2. Current studies often have a small number of participants, are not easy to replicate or have other important limitations.	- Difficulties to understand patients profile/characteristics; patient selection is not optimized - Used technologies are not extensively described, making it hard to replicate it - Gap between medical publications where focus is on clinical achievements and engineering publications where focus is on technology itself –need to close the gap in a more comprehensive way of both fields? - Need for better and continuous collaboration of both fields (engineering are often responsible for research and development of technology and medical has access to patients and knowledge of clinical pathways) – this may also improve medical scepticism towards technology they don't fully understand - Lack of standards/guidelines for reporting complex clinical approaches like the use of BCIs

3. Regulatory approval of this devices for clinical use will not ensure these devices will be able to be reimbursed for the patients who might benefit for its use.	- Roadmaps or guidelines through all the research and development processes should be in place to assure both these approvals are obtained. - A change in the regulatory bodies to ensure more flexibility and easier understanding of what is needed for both the regulatory approval and reimbursement might help? By creating a new "agency" for neurotechnology, for example, instead of current regulators more adapted to drugs. - Need for long-term monitoring
4. Funding programs and research grants benefit novelty and promising research that promises breakthroughs over sustained research on the various development stages need for BCIs to enter clinical practice.	- What is the role of academia and how may it approach solutions for translation to clinic? - Partnership between public and private sectors may be a solution? - Breakthroughs in BCIs are being achieved today by researchers working in a largely siloed manner across multiple disciplines and disease areas. How to improve collaboration between research groups, companies, etc?
5. Artificial Intelligence (AI) may play a major role on the future of BCIs.	- More safety (redundant mechanisms as safety contingency) and reliability (more data will bring improvements) - Data privacy and security (who owns, who stores, who may use)
6. Society perceptions will play a role in large-scale adoption of BCIs.	- Does society still connect BCIs to science fiction? - Previous hype around these devices might damage their reputation? - Look and aesthetics, usability, autonomy, etc is key to the patients (end users) - Key role of patients and caregivers in all research and development process.

The Questioning route was predetermined and idealized to promote interaction between participants. Moderator commenced the focus group by asking broad questions using the polls created, before asking participants to reflect and comment on focal questions(49). Although participants individually answer the facilitator's questions, they were encouraged to talk and

interact with each other, based on the notion that the group interaction encourages respondents to explore and clarify individual and shared perspectives(49). The focus group tone was informal and, to maximise participation, there were open spaces for the participants to add topics or ideas that weren't in the route.

The focus groups were recorded and later transcribed using an automatic speech to text tool. When there were mistakes that might interfere with the text comprehension in the transcription, the authors corrected these by reviewing the record.

3.2.3. Data analysis

Quantitative data obtained from the polls and its questions, with answers using a 5-point Likert scale, the results from the three focus groups were aggregated on a Microsoft Excel spreadsheet (Microsoft® Excel®, Microsoft 365 MSO (version 2202 Build 16. 0. 14931. 20128) 64-bit) and these aggregated results are presented in graphs in section 4 "Results".

The qualitative analysis of the discussion is described in aggregation of the three focus groups, in a narrative way. The approach to analyse, synthetise and report data, included a 32-item checklist: Consolidated criteria for reporting qualitative research (COREQ)(49), which may be consulted at Appendix 3.

3.2.4. Potential bias

A selection bias may be present due to participant sampling, as these were selected by purposive sampling and all the participants had previous contact and knowledge of Neurotechnologies. Not all the stakeholders in the field of BCIs and neurotechnology were addressed which implies that not all points of view are taken in consideration.

A perception bias may also present. Some of the participants had previous contact with each other and have worked in the same projects, which can lead to "think-alike" and reduce discordant opinions.

Small sample of this study may be inadequate to reflect all points of view regarding the aim of this work, therefore results must be looked carefully.

As this is an exploratory work on an emergent field, the inherent publication bias and the influence this had on this study construction and reflection on the theme, must also be taken in account.

4. Results

4.1. Summary of systematic review findings: potential clinical applications of BCIs in humans

BCIs may bypass non-functional corticospinal pathways to allow for the brain's control of technical devices to assist in daily life activities or facilitate neuroplasticity within the CNS (central nervous system), and in particular, the brain thus aiming at movement restoration by enhancing motor learning and motor recovery(52).

Main roles of BCIs in rehabilitation are replacement and restoration of lost neurologic function(53). BCIs are used to replace lost neurologic function by restoring patients' ability to interact with and control various environments and activities, environmental control units, mobility devices, or neuroprosthetic limbs and orthoses(53). They can also be used with rehabilitative therapies to help restore normal central nervous system function by synchronizing brain activity that corresponds to movement intent with actual movements and sensations generated by end-effector devices, inducing brain plasticity(53).

BCI systems have emerged as one of the promising tools for motor function restoration(33). In spite of the success received by BCI-based interventions in the motor domain, non-motor impairments are yet to receive similar attention in research and clinical settings(33). Other applications of BCIs include improving voluntary movement control and reductions in spasms and pain, proving this technology multivalency in healthcare contexts(53). Of relevance, useful and novel applications developed in this domain may contribute to the evolution of technology in healthcare and help to improve patients' QoL.

BCI combined with a wide range of different interventions reflects complexity and variety in of its applicability(54).

Invasive BCIs, due to its capacity to extract neural activity with higher spatial resolution, have the potential to provide richer information about the person's movement intent, thereby enabling faster and higher accuracy communication than non-invasive methods(55). Another advantage of a chronically implanted BCIs is the relatively quick and easy daily setup compared to non-invasive methods(55).

However, the chronic implantation of electrodes and associated components carries risks associated with long-term degradation of the device and surgical implantation, therefore, non-invasive BCIS have a safer profile(28,55).

Current BCI systems are not well suited for use outside the clinic or research laboratory due to their large size, high costs, lengthy set up time and requirement of highly trained personnel(54).

4.1.1. Applications in motor rehabilitation

BCIs have been used as investigational assistive devices for individuals with chronic paralysis from multiple causes, including cervical spinal cord injury (SCI), spinocerebellar degeneration, amyotrophic lateral sclerosis (ALS) and brainstem stroke(53).

BCIs can help people with limited mobility by monitoring their neural activity, enabling them to control devices(28). Nowadays, most BCIs help people with severe movement disability by replacing or restoring lost movements, including BCIs for control of prosthetic limbs or spelling systems. Thus, people who can no longer perform abilities like grasping, typing, or speaking can replace lost functions by directly controlling a device with brain activity(54,56–58).

For compensation of motor impairments with the use of BCIs, the preferred target population is the group of high-lesioned, tetraplegic patients with motor complete SCI because of the limitations of traditional user interfaces(52). Although evidence is sparse, rehabilitative BCIs may represent a valuable adjunct therapy in patients with partially preserved motor functions, in the subacute phase after injury(52). Current evidence also indicates that, for a subpopulation of individuals with SCI, an anatomical change and functional reorganization process might occur both at early and later stages within the cortical and spinal regions(52).

Subjects with tetraplegia have achieved success to enable BCI control of a robotic arm that to intuitively control the position of the hand, the orientation of the wrist, and simple grasp configurations(53). Invasive BCI is a viable control mechanism for chronic tetraplegia, performing well >4 years after implantation and expected to confer greater independence for self-care(59).

Direct neural control of assistive technologies through BCI could also tap into otherwise unused but well-functioning brain areas (e.g., those formerly used to control speech or arm and hand movements) to provide natural, intuitive control over assistive devices(55).

Invasive BCIs have also shown good results in using brain signals to offer an alternative way of communicating or control devices for people with LIS(55,60). This approach has also proved the rich information content that can be extracted about movement intention using invasive BCIs enables high quality neural control to be obtained within minutes of beginning decoder calibration, with little or no training required on the part of the user and minimal cognitive load(55).

BCI results seem to differ sharply between patients in LIS(21). Several BCIs have been developed to provide a means of communication to paralysed patients, with most reports focusing on ALS patients in different stages of disease progression(21).

Persons diagnosed with ALS may use different strategies and several devices throughout the course of their disease(61). Current BCIs can extend the continuum of Augmentative and Alternative Communication (AAC) assistive technology efficacy beyond its previous limits(61).

Invasive approaches have shown the most promising results in LIS, with reports demonstrating relatively fast spelling of words(21).

LIS in patients whom suffered a brainstem stroke is also a condition addressable by BCIs(60). A recent study has showed that high-density recordings of cortical activity in the speech-production area of the sensorimotor cortex of an anarthric and paralyzed person can be used to decode full words and sentences in real time, when conjugated with deep-learning models and language-modelling techniques, to decode a variety of meaningful sentences(60).

The recent development of BCI tools to target cognitive and motor impairments has led to the exploration of these techniques as potential therapeutic tools in patients with traumatic brain injury (TBI)(62). Only a few studies explored the effects of BCI interventions in conscious patients with TBI, which allow no conclusions regarding the applicability and efficacy of such techniques in clinical practice at present(62).

Motor rehabilitation is the most researched application of BCI in the stroke domain and restoration of upper extremity motor impairments in stroke patients served as initial motivation for the exploration of BCI technology in the post-stroke rehabilitation field(5,33). The use of BCI based rehabilitation has shown to outperform most conventional forms of treatment(5,33). They have performed arguably better at engaging the user and achieving better functional outcomes than any other contemporary rehabilitation therapies(57).

Studies also showed that BCIs seem to be safe for patients with stroke(5,27). Meta-analysis also showed a trend that suggested BCIs were effective in improving upper extremity function(27).

Quantitative analysis showed that a BCI training in patients after stroke was effective for motor function recovery of the upper and lower extremity, while also enhancing brain function recovery(54). Upper-limb therapy resulted in improved motor function for patients with chronic stroke, as determined from post-treatment assessments(57).

Using BCI, a patient performed skilful and coordinated grasps and made clinically significant gains in tests of upper limb function(59). Practice generalized from training objects to household items and leisure activities and patient showed improved motor ability for palmar, lateral, and tip-to-tip grips(59). It is expected eventual home use to confer greater independence for activities of daily living, consistent with observed neurologic level gains(59).

Upper limb motor function improvement after 12-session BCI intervention was shown in the BCI group compared to the control group(63). Another study found that subacute stroke

patients after BCI training not only showed better motor recovery, but also activities in other brain networks, including somatosensory, visual spatial processing, and motor learning(64).

Studies benefits in training, monitoring, calibration, and motivation in stroke patients that may lead to inherent improvements within the rehabilitation processes, however studies corresponding to lower limb rehabilitation were a minority(3).

Most studies demonstrated that the integration of BCIs with visual, auditory and/or haptic stimulation is useful and increases the efficiency of the interface in rehabilitation, since it enhances the physiological and emotional effects of the person(3).

Although there is evidence showing that BCI together with physical practice (conventional therapy or robots) can enhance upper limb function recovery, it is still unclear how it promotes clinical and neurophysiological changes in stroke patients in the long-term(56).

4.1.2. Applications in sensory restoration

Besides motor deficits, stroke patients also frequently suffer from cognitive impairments(33).

Some preliminary encouraging results in post-stroke cognitive rehabilitation using BCI seem to suggest that it may also hold potential for treating non-motor deficits such as cognitive and emotion impairments(33). Moreover, past studies have shown an intricate relationship between motor, cognitive and emotion functions which might influence the overall post-stroke rehabilitation outcome(33).

The critical nature of somatosensation in motor control is also a topic being address with BCIs in amputees, reducing lower-limb pain and improving sensory feedback(53). BCI provides a novel method to directly change the information content of motor representations and to control phantom limb pain(65).

Significant ongoing work is aiming to at create sensorized prosthetics that can provide the information necessary for stimulation(53).

4.1.3. Other applications

Still, in the cognitive field, trials demonstrate that BCI is a promising approach for treating people with Attention Deficit Hyperactivity Disorder (ADHD), by normalizing their abnormal electroencephalogram (EEG) patterns(66). This trial showed BCI is not inferior to medication and its efficacy is increased in combination with pharmacological methods(66).

BCIs can also be used in disorders of consciousness (DOC), like comma(55,67). One of the most important issues to families and loved ones of motorically nonresponsive patients is whether or not the person is still conscious(55). Reports have described individuals who had been

diagnosed as minimally conscious or in a vegetative state showing some signs of activation in brain areas of communication and movement(55,67).

BCIs can be useful for DOC patients in potential awareness detection and command following, while some patient groups can also greatly benefit from BCI applications for communicating and controlling their surroundings with assistive technologies, which in turn could give users their autonomy back and improve their quality of life(68).

BCIs also seem to be taking first steps in diagnostics. One study reported this device may be useful for assessing the electrical brain responses associated with visual field stimulation, discriminating eyes with glaucomatous neuropathy from healthy eyes in a clinically based setting(69).

4.1.4. Summary table of findings

Previously reported findings have been synthetized according to BCI potential application to clinical conditions in Table 7.

TABLE 7 | Summary table of potential clinical applications of BCIs in humans

Applications in motor rehabilitation	Applications in sensory restoration	Other applications
Control prosthetic limbs	Help treat cognitive impairment	Help treat ADHD
Spelling systems	Help treat emotion impairment	Assist patients with DOC
Rehabilitation of motor functions	Sensorized prosthetics	Glaucoma diagnostic

ADHD: Attention Deficit Hyperactivity Disorder; DOC: Disorders of consciousness

4.2. Empirical work: focus groups on barriers and opportunities for the use of BCIs in clinical contexts

In this section, aggregated results obtained from the focus groups are presented. Both the quantitative and qualitative results are presented in the order they were discussed during the focus groups.

Quantitative data from the polls is firstly presented, followed by the qualitative date generated from the discussion after each poll's question.

Answer rate in percentage for each focus group and for each statement individually was calculated. The answering rate mean for the focus group was 85,5% (lower: 76,4%; higher 93,3%), with a standard deviation (SD) of 8,5%; and the answering rate mean for statement was 82,6% (lower: 72,7%; higher 90,9%), with a SD of 6% (Figure 8).

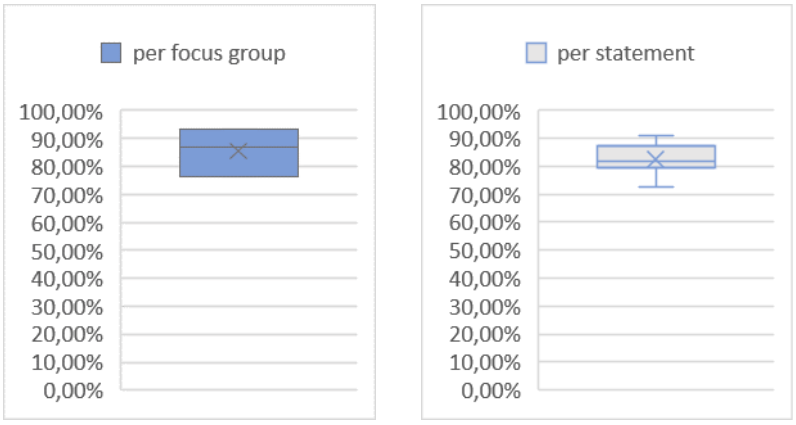


FIGURE 8 | Mean and SD of answering rate per focus group and per statement

4.2.1. Aggregated quantitative results from the focus groups polls

Regarding the beginning of our focus group and the first poll statement: "BCIs have the potential to be a solution for some current unmet clinical needs.", we saw most of the participants tended to agree (strongly agree: n=8, agree: n=8), as shown in Figure 9.

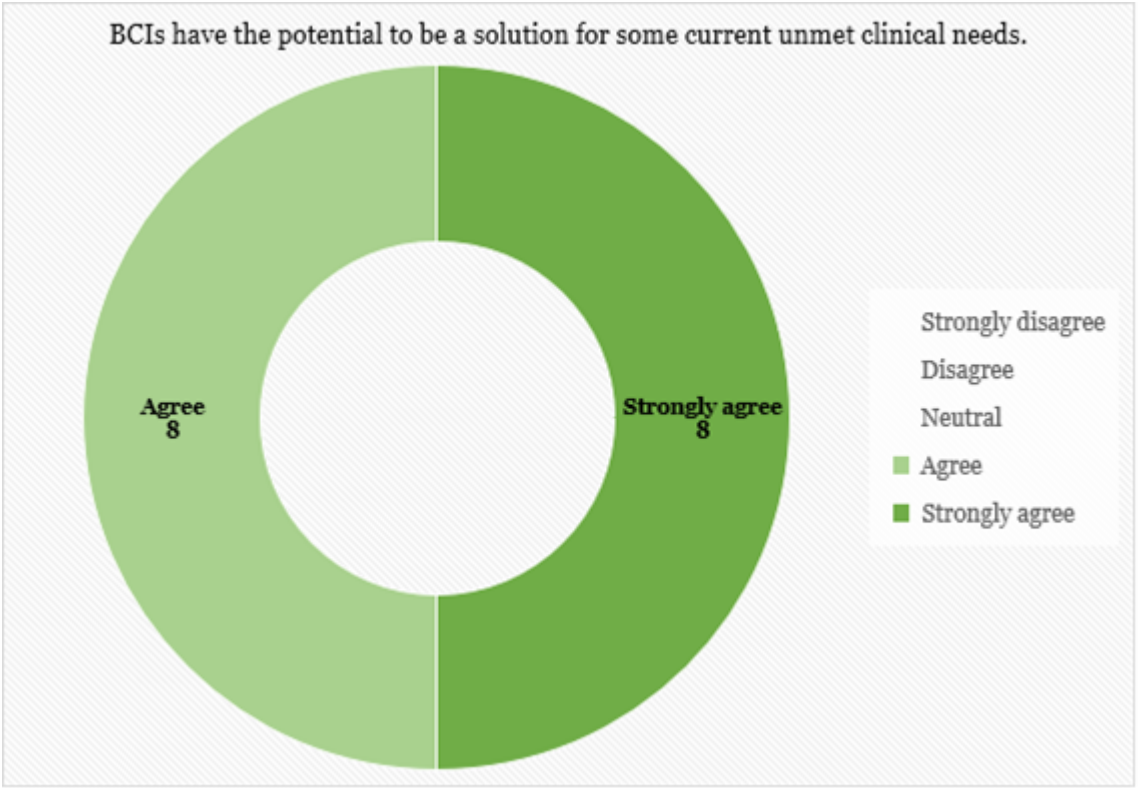


FIGURE 9 | Answers to the first statement

First remark for the opinion on the need to better define BCIs. It is important to notice BCIs may be classified according to different perspectives like, for example, invasive or non-invasive; assistive or rehabilitative; based on acquired signals, between others. Here we assumed BCI as an umbrella term and opt to specify what type of BCI, when needed.

Continuing the discussion, the second poll sentence was introduced: "Current studies often have a small number of participants, are not easy to replicate or have other important limitations.". Once again, the participants showed a high level of agreement with this sentence (strongly agree: n=5, agree: n=15) (Figure 10).

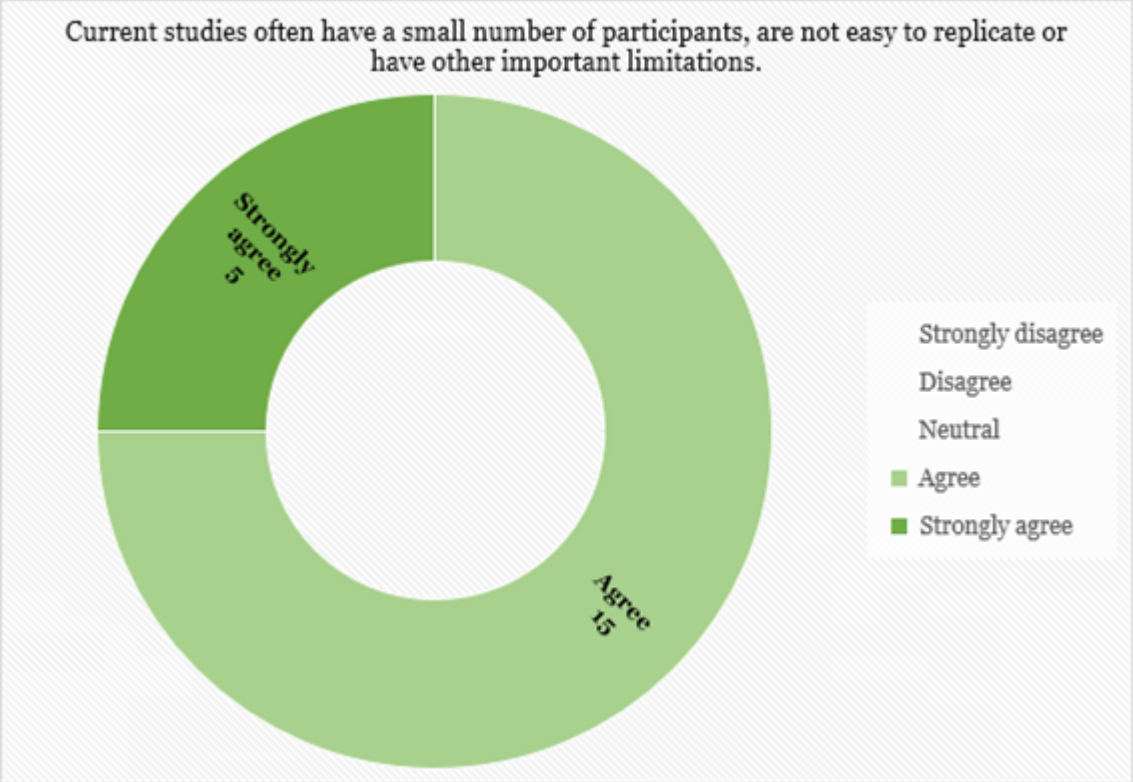


FIGURE 10 | Answers to the second statement

The third statement was: "Regulatory approval of this devices for clinical use will not ensure these devices will be able to be reimbursed for the patients who might benefit for its use.", and in this case most of the participants remained neutral towards the statement (strongly agree: n=2, agree: n=5, neutral: n= 10; disagree: n=1) (Figure 11). Most of the participants justified their neutrality with low knowledge and unfamiliarity with this specific topic and, therefore, they did not feel comfortable to classify the statement.

After some discussion, the focus group continued with the fourth statement: "Funding programs and research grants benefit novelty and promising research that promises breakthroughs over sustained research on the various development stages need for BCIs to enter clinical practice.", which showed a more distributed opinion with a slight disagreement, although most of the participants agreed (strongly agree: n=6, agree: n=10, neutral: n= 1; disagree: n=2) (Figure 12).

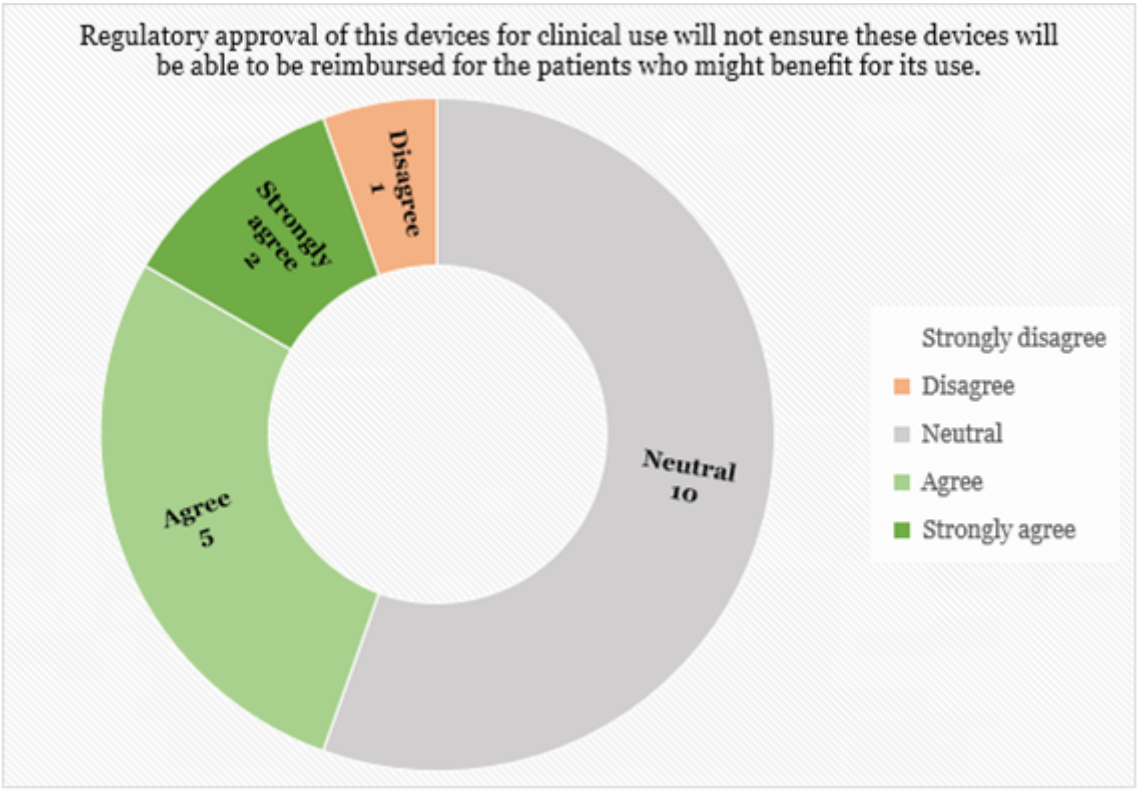


FIGURE 11 | Answers to the third statement

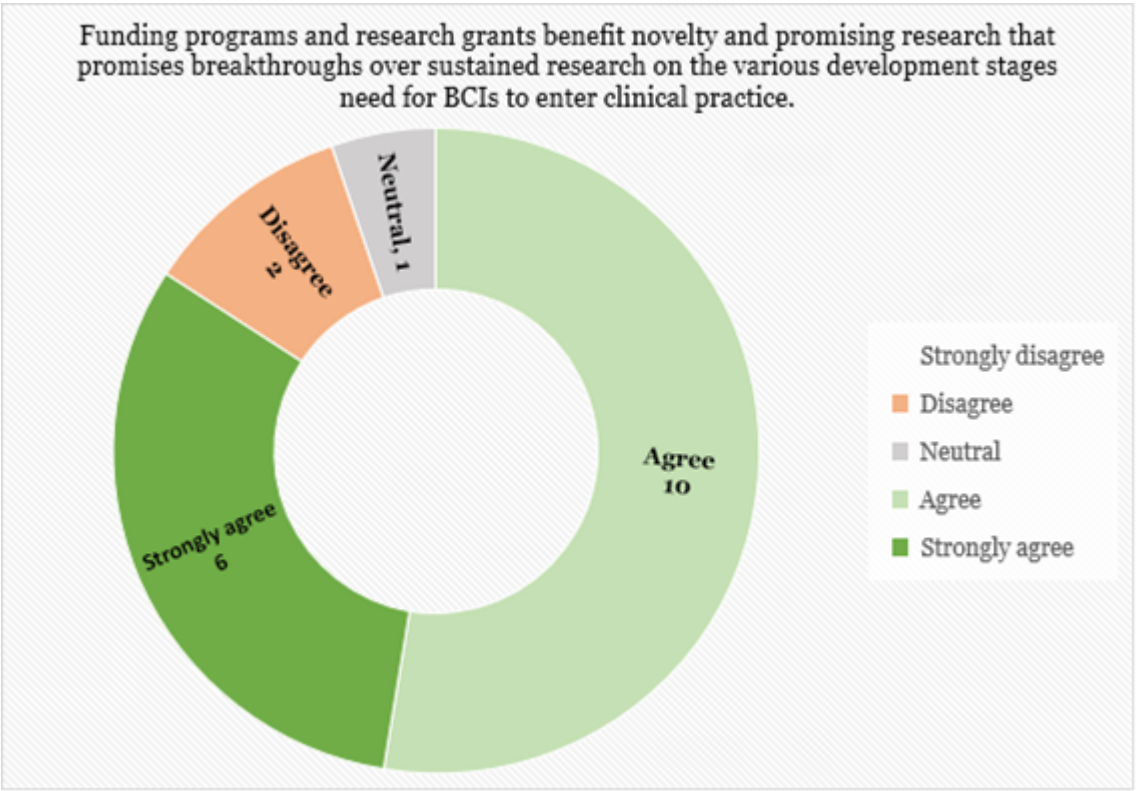


FIGURE 12 | Answers to the fourth statement

In fact, most of the participants agreed that there is a certain pression to publish new and enthusiastic discoveries instead of improvements in previous works. On the other hand, some participants pointed this is not totally accurate and there is space for publish and receive funds on studies that show a significant improve in some previous work as long as the new one shows the importance of this improvements on same spheres that might include - but are not limited to - usability, better performance or accuracy.

The moderator then introduced another poll: “AI may play a major role on the future of BCIs.”. This statement showed also some more distributed results, with answers going from “strongly agree”: n=6, “agree”: n=9, “neutral”: n= 2, to “strongly disagree”: n=1; as show in Figure 13.

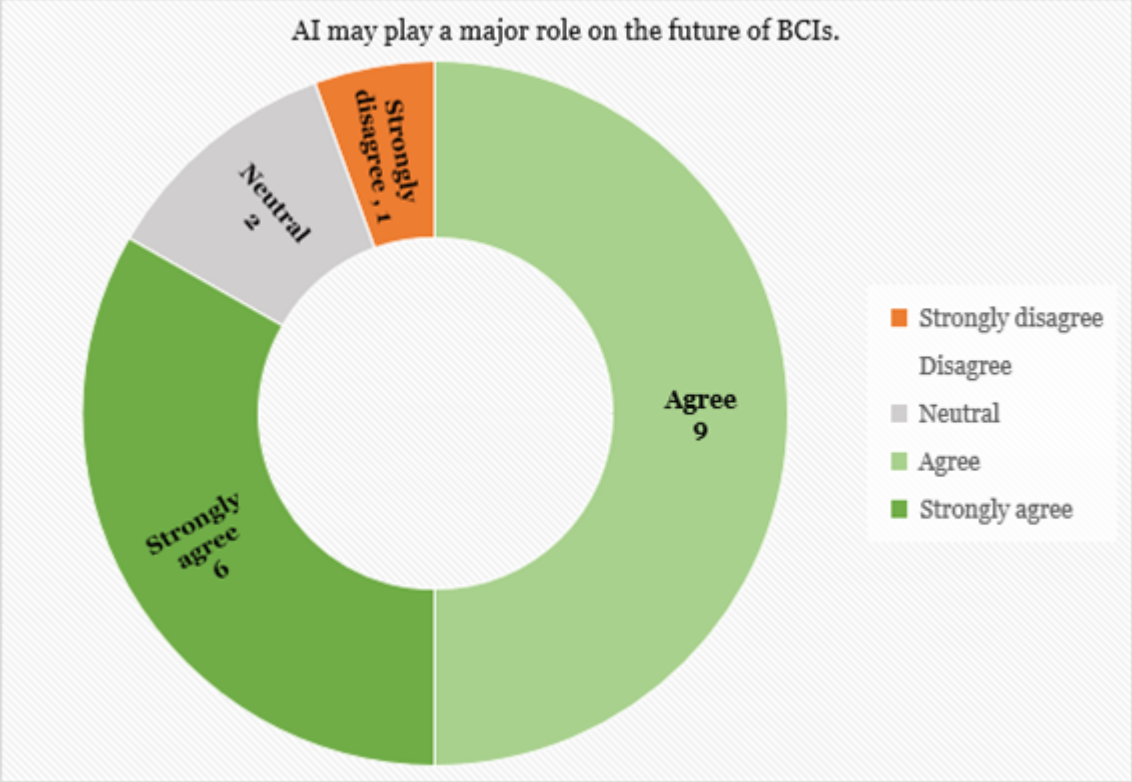


FIGURE 13 | Answers to the fifth statement

Some participants stressed the need to define AI (algorithms, machine learning) and to be more precise in what way we were thinking about its usage, namely if we mean to incorporate AI to analyse the signals and data directly collected from the brain or to use AI in end effectors or applications related and controlled with a BCI, as this may have different interpretations. Once again, it was showed the importance of terminology and to get better and more comprehensive definitions in this field.

Approaching the finish, the last statement was introduced: “Society perceptions will play a role in large-scale adoption of BCIs.”, to be classified. This statement also showed more dispersity in the results with answers “strongly agree”: n=5, “agree”: n=8, “neutral”: n= 3, “disagree”: n=1, and “strongly disagree”: n=1 (Figure 14).

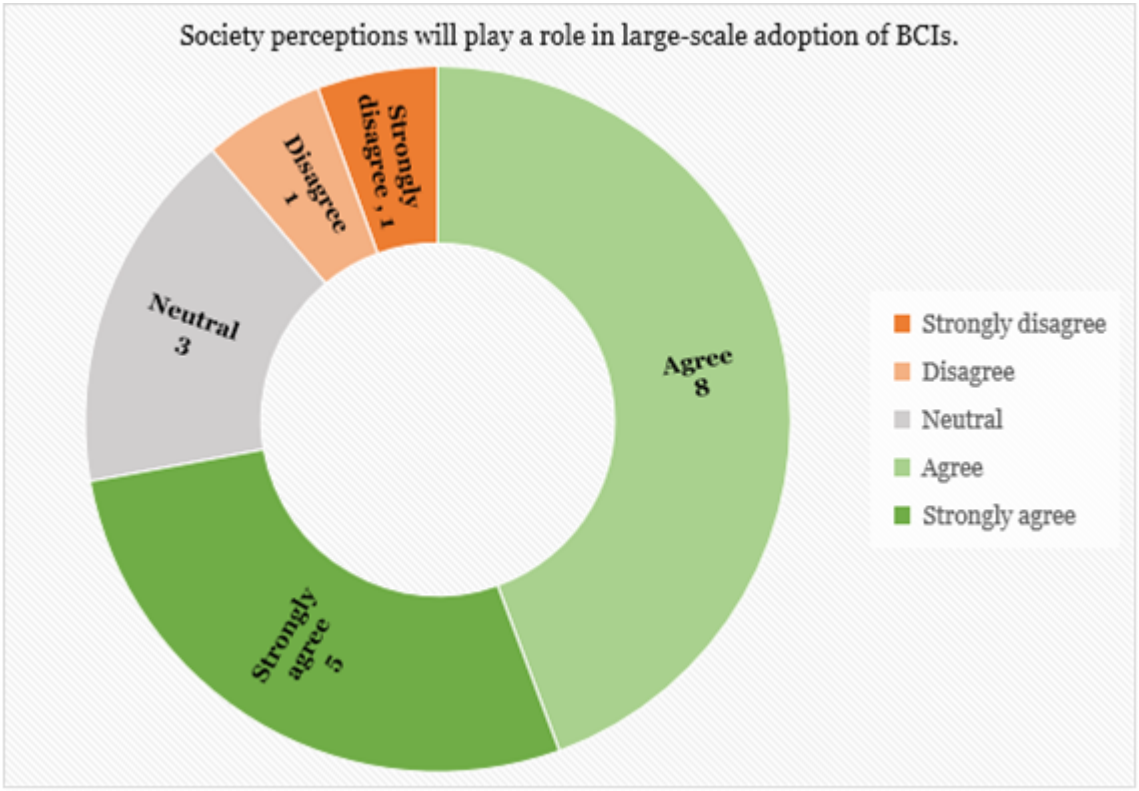


FIGURE 14 | Answers to the sixth and last statement

This was a premise of the importance of cultural context and the different contexts of the participants, showing that when implementing solutions, one should always have in mind the regional background and understand the societal context where the implementation is occurring, taking a more contextual approach instead of going into generalizations.

4.2.2. Aggregated qualitative results from the focus groups

In summary, there are two major issues to get over and adopt innovative technologies. The first valley of death is the translational and it is about market forces in the translation of technology to the clinic (typically first in human or small studies already seen with BCIs). The second includes clinical adoption and market forces to be able to commercialize the device.

Part of the issue could be the fact there is not a true use case of how to implement a BCI to a particular population, so BCIs have been developed within a medical model but there is still the need to figure out use cases that might not totally fit this model. Talk with people already using BCIs and talk with the target population with potential for being served by these devices are distinct aspects of BCIs implementation. The gap in the translation to the clinical settings proves there is still work to do between the phase of idealization of a tool and its use in a real-world context.

The current picture of technology devices and neurotechnology in Health call for the integration on engineers and other professions that are usually not so linked to healthcare. These professionals may also play a role in improving healthcare professionals' technological literacy

and this will surely add value to the health field, bringing not only new options of diagnosis, treatment, management of disease but also improvements at structural level. Nonetheless, this impact and the need for integration of different areas of knowledge will always vary between regions, so each country should plan a personalized approach based on its context and needs. Still, collaboration, teamwork and development of a common language will always be key, and a sooner integration of all stakeholders at the beginning of any project is of major importance.

Healthcare is a market known for taking time to adopt technology and to drive change and unless the technology is proved safe and with clinical impact, it will not be adopted. Costs must also be taken in account and a connection to benefits must be proven. At the end, healthcare professionals will want the best and right, or the most suitable option for the patient and a proper use of the technology combined with robust evidence and best cost-benefit ratio will make BCIs an option to consider for sure. More studies are needed, a better comprehension of brain mechanisms, HTAs and guidelines for practitioners may help to drive adoption.

When technology seems to be too futuristic or too advanced, people think that anything could be done quickly in a couple of months and they expect engineers to come back with the device able to restore capabilities of the person, which is not possible, so there is the need to avoid disappointing the patients and to avoid disappointing the clinicians. To create trust and build a relationship between researchers, patients and their caregivers (including doctors), addressing potential issues and being pragmatic about BCIs, so projects could advance with confidence and best possible results.

Translate BCIs to hospitals will need doctors, and they would like to be involved and being listened in the user centred design process, they want to know that the user requirements are clear according to their point of view for avoiding mistakes, but they also have a role by stimulating and engaging patients and that psychological effect is very important for researchers and engineering professionals developing neurotechnology.

4.2.2.1. Research related perspectives

The development of devices like BCIs are in the boundary and intersection of, at least, two distinct scientific fields: Medicine and Engineering. The technological specifications and all the technological development as well as guidelines to report these may be not interesting for journals publishing about medical subjects. Technological aspects of BCIs are often published on journals with lower impact factor related to Engineering fields and less known to health professionals. On the other hand, medical journals with higher impact factor will publish work more focused on the health applications of technology, leaving specifications on the background.

From the engineering side, there is often the feel that their R&D work before the use of the device is not valuable or does not share the same scientific appreciation from Medicine as other interventions. In this perspective, even if the technology is robust, to get it on a clinical trial will still be hard as for regulators technology development is not qualified as “science” from for

example drugs development and biological discoveries. In this matter, there is still the need to "sell" neurotechnology devices to the scientific community so they might be considered as a potential therapeutic agent.

The publishing industry and how it seems to give more importance to novelty instead of continuous improvement of already existing solutions was also mentioned as a point of interest. This makes hard to understand questions that remain open in the publications and that are not addressed in follow-up papers. This leads to the fact that incremental research is often not valuable, giving more space and hype to the novelty of some technological advance, but failing to support continuous improvement and the development of BCIs that will be ready to enter the healthcare ecosystem.

The need for collaboration between professionals from different areas during the R&D of the technology and all the research is also referred as a key point to success. The intersection between engineering and medicine areas calls for an approximation, share and cooperation between all the professionals involved to enhance technology itself and its potential use in patients. Guidelines and standards to comprehensively report neurotechnology interventions are welcomed and there are already some groups working on it.

At the moment, BCI technology seems to be at a good stage and current problems are addressable with current knowledge. However, conciliating it with medical and clinical outcomes and expectations is harder. Health professionals may play a role in understanding and conciliate objectives from both sides of research, enhancing trials design to evaluate relevant outcomes for the patients. Fulfil the diverse goals of a multidisciplinary team and understand how to integrate engineering improvements into clinical benefits is a challenge which is visible in most of the current literature.

A concern for both health and engineering professionals is to understand patient profile and understand what characteristics may have influence on the system performance and consequently on the outcomes. Building up on previous comments, the need for patients' engagement with the technology and motivation play a role in the final result, so steps that will improve both engagement and motivation will mean the patient would be prone to put more effort on training and learning which in turn will lead to better and more significant outcomes. However, to fully understand these topics is difficult and a more comprehensive approach to reporting all the steps of research may improve overall view and perception.

More research both on the technological and clinical side, with the understanding of what pathologies and patients will benefit from an intervention with BCIs, and on usability is an important step. There is a huge effort in terms of technology as far as BCI is concerned but very few serious studies trying to understand how to encode or decode the brain signals, so even with a system with lots of electrodes, it is difficult to really know and understand what to do with it because we are not still at the point of totally understand the brain and its mechanisms.

However, it is not mandatory to understand all mechanisms of action if there are proven significant health outcomes for the patients, but it will certainly help in gaining clinicians confidence. To have a long-term monitoring system for all the patients using BCIs may help addressing concerns and get more information about its long-term effects.

Technical issues that must still be addressed also proved to be a barrier to overcome when translating BCIs to clinical context and with its further scale up. These issues included, but are not restricted to, electrodes, connectors and consequent assemble of the entire system to function according to expected and to be at the same time cost-effective providing the best solution to the patient problem. Concerns on how implantable devices (in the case of invasive BCIs) would maintain function and reliability over the time are also important to be addressed by the technological side. Still regarding technology, it is hard to ensure the reliability of BCIs from one to another, as the process of development and production of these devices is still not totally standardized and industrialized to a point where it can be easily and accurately produced in quantity. Keeping the topic of reliability there were also opinions expressing that, in some cases, BCIs may not be reliable enough for the patients' expectations, leading to premature abandonment of these devices. A point was made relating this issue with non-invasive devices, which have a low signal quality.

On the other hand, there is also a problem with sharing data of patented (or waiting for patent) technologies and the lack of guidelines for reporting the needed data to evaluate these devices does not help stakeholders to understand what is really needed to share to achieve clinical trials without putting intellectual property (IP) at risk. One participant added that although this is generally true, in most recent papers there has been more care to provide accurate and more data on all the technology used as well as more information regarding the population. Even if these data are not represented on the main body of the paper, it is usually present as supplementary material.

Sample size of the studies is an issue, preventing clinicians from having more trust in BCIs, but it is also important to remember that sample sizes may be limited to external factors. Patient recruitment is mentioned as a difficulty in the research phases. Improving awareness around BCIs and more collaboration across institutions leading to tighter relations across all the stakeholders may bring innovative approaches to clinical trials and systemic barriers to this kind of technology.

One key point made is that if the outcomes of BCI technology are like to improve QoL or reduce disability and really have the possibility to have an impact of one's life and on society and productivity it is more likely to adopt this new technology as it will be seen as more relevant by the general public or society, having a bigger possibility of being reimbursed. Although reimbursement for these devices is not yet a reality, multiple papers have already shown the importance of BCIs to improve some patients QoL. These papers also focus on patients' needs,

what they value the most, their opinion on design and aesthetics, also showing the importance of integrate patients in all R&D phases of this kind of neurotechnology.

The aspects of improving patients' life have been addressed in many ways and there are already entities demanding patients' integration and consultation when applying to grants or submitting projects to regulator and payers. We should have in mind researchers often fail to totally understand the main priorities and needs of the patients and, having their input, may change the result, contributing to technologies more adapted to real world patients and needs.

Continuous funding is a hurdle. The problem of obtaining sustainable funding for continued research and improvement of these devices is a real struggle. When obtaining public grants for funding research, it is easier to sell a project of a promising scientific breakthrough or something novel in the field. This creates a gap between initial funding and continuous funding to bring devices like BCIs to a step where it is ready for large adoption.

Regarding grants and funding programs, which are responsible for most of the initial investment in healthcare technology development in academia and research centres, there seems to be a balance towards the encouragement of breakthroughs and novel discoveries. This seems to be a practical problem connected to a publication bias as most of the journals will be more interested in publishing breakthroughs than experiments showing that a device was able to be safe and stable to use for a long time. A more balanced approach to public funding, with a clear strategy that allows breakthrough discoveries and translation projects to be funded will certainly help BCIs systems to achieve healthcare sooner. Some governments grants and entities seem to be already addressing this issue, having specifical grants for basic research, for translational research and for breakthroughs advancements, and putting a bigger emphasis on the potential societal benefits of the discoveries. These seems a more balanced approach towards a sustainable and continuous improvement research model.

Public funding may be the first step in funding research of devices, but in the medium and long term, partnership with private entities may bring value and add the extra step in bringing neurotechnology devices to patients, scaling up and making it wide available. However, there are some steps being taken already. Grants for medical translation and research councils focusing on applying technology to Health are already a reality and may help bringing a wide scope for BCIs to achieve clinical settings. Funding landscape is evolving and bringing more stakeholders to the table, somehow mirroring what happens in private companies that develop technology.

In the private sector, there will always be ask of investment return and the need to make some profit from the devices developed, which will be high dependable on commercialization and reimbursement of BCIs systems. On the other hand, the private sector is often more willing to accept risks and to invest more. To understand the size of the market and how many patients will be willing to use or buy BCIs is still a major question. One thing that may enlarge

opportunities is also to seek for new applications of these devices and promote their usage not only for patients but for people that may be temporarily "impaired" (for example a parent may be "impaired" for one arm because of being constantly using that arm to carry its child). Of course, this case falls out of a clinical use and therefore will imply BCIs as a consumer technology, but it this direct-to-consumer strategy is already a reality for non-invasive BCIs and may help to fund companies and allow the development of "clinical" BCIs.

Nowadays, researchers working on making BCIs available to the public are asked to have a clear commercialization strategy and leave academia behind to create their own start-ups to conduct research beyond the laboratory or they will lose control on the future development of devices as they are not trained to think how to evolve beyond and after the IP stage. One idea is to make students go to research departments of different scientific and technical areas and learn most of the global picture so when the time comes, they are more lettered on the global picture of medical devices development and translation. Including companies in the research centres, in academia, and improve the spirit of collaboration in the development process and in the healthcare, pathway may improve translation and commercialization on the long-term and be an effective way to intersect and integrate knowledge.

Bringing together academia, research centres and enterprises in collaborative projects may help, not only addressing this issue, but also work as a catalyst to the development of multidisciplinary work relationships. To work on a local infrastructure, in a known environment may also have positive impact, at least at the beginning. On the other hand, it is important to understand these projects more focused on a final application will not be so innovative, so a balanced approach between new technological discoveries and application of the current tested devices into clinics will be needed.

4.2.2.2. Healthcare ecosystem related perspectives

Whether talking about invasive or non-invasive BCIs, regulation and reimbursement hurdles, will always come into play. Recently, a lot is being done in terms of research and regulation may come as the nest bottleneck with huge differences across the world.

When developing strategies, it is of major importance to think about the healthcare system itself. There are great differences in the reimbursement process and in the regulatory background in different healthcare systems, so pathways must be clear for each one. For example, to get a device approved by FDA and reimbursed in the United States of America (USA) is different from getting a device approved according to European Union (EU) Medical Devices Regulation (MDR) and reimbursement is also different within EU countries. Depending on the country, the device high cost (especially the invasive ones) may still be a barrier as the health system may not be able to pay for such a fee. As a result, when developing BCIs, is important to have in mind the final cost of that device and although companies may have this information, usually there is no research on the economic part of it.

As seen in several studies, sometimes the engineering part of BCIs development is trying to make the most "fancy" or evolved device, but as an all, the more crucial point is to think about its function and outcome reflecting it in a cost-benefit way. It is important to distinguish when certain materials and a certain number of electrodes and connectors are useful or not and if they real bring benefit when going to the clinical trials. This trade between getting the "best device" or the most useful device shows the importance of having interdisciplinary discussions from the beginning as understand the final goal and the best way to achieve it without get an overcomplicated system or device.

For some countries, the regulatory bodies already recommend the report of some standards measures and require QoL assessment questionnaires for the approval of clinical trials of devices for chronic patients. These same measures and assessments are also part of the reimbursement process, which clarifies and simplifies both processes for the teams responsible for R&D of these devices. This seems already a good strategy and one good step towards a framework to simplify the pathway to access the healthcare market.

Regulatory bodies remain conservative when conceding approvals for medical devices and this is no different in the BCIs case. The fact the brain is involved is also a factor to weight in. One strategy, from a regulatory perspective, may be to go in steps. To introduce features of implantable devices, thinking about its safety first and then going on to start arguing the benefits and introducing smarter sensing, closed loop capabilities, AI tools, etc, might be a long but promising pathway for implantable chronic implantable devices.

Another way, which has already been adopted in some countries, is temporary reimbursement of medical devices through a fast-track process after they complete the regulatory process, permitting to continue to build evidence and generate money for the companies to survive and continue to improve their device. This approach is not consensual as there is the argument that long-term safety of the devices approved is yet to be proved. On the other hand, it may be of importance to some chronic diseases that have no current treatment or acceptable solutions for the patients, and it contributes to generate more evidence on the device and allow for a long-term monitoring of its features in a real-world scenario, improving access from patients otherwise will not be able to enter a clinical trial or a study.

Fast-track programs, for regulatory approval and reimbursement, which assure payment for a certain amount of time when the device reaches technological maturity and has been tested for security and feasibility, proving significant clinical outcomes in a defined sample and with a plan for monitoring throughout its usage, may help adoption and scale up in healthcare.

Effective communication and partnership between engineers, who are responsible for most of R&D stages of BCIs, and health professionals, who will be responsible for accessing user requirements and patients' limitations and needs, is very important to pave a way for the development of a project that meets patient needs and has the right outcomes measurements.

Throughout all the process, a continuous communication with patients to have input and understand needs and values will certainly contribute to the creation of devices that have a better shot for being approved for medical use and reimbursed. Again, a framework integrating all the steps and all the stakeholders might lead to better and more purposefully research, achieving BCIs translation and scale-up into clinical settings.

Regarding doctor and engineers, it is also important to set clear expectations and goals on what both areas want and what is possible, leading to a commitment. These goals, expectations and current state-of-the-art must also be discussed with regulators so all may work together towards a common goal and achieving the best solutions possible.

Patients' role in regulatory approval and the path for reimbursement cannot be disregarded. Performance indicators of BCI technologies and patients' opinions are pieces of a puzzle and it seems there is lacking guidelines or paths that point a strategy to develop BCIs that may have potential to be translated into clinical settings. Patients are still humans, and, for some people, this will mean to be creative, to be connected to arts for example. One interesting idea is that any patient is different and while, for example, one person with ALS might want to use a BCI to communicate through words appearing on a screen or synthetised by a computer, for another person with the same pathology, artistic expression by drawing or making a sketch may be more important to her happiness. This is an example of how BCIs should and might allow a tailored approach to each individual, while using the same hardware.

There is the risk for researchers to think of something that in reality may not express or not meet the real perspectives and needs of them. To really prove in a scientific way that research is bettering patients' QoL and to generate evidence to regulatory agencies and to apply for reimbursement is a tricky field, and if BCIs will not be reimbursed, that will affect its adoption. How to measure QoL, the health economics of restoring patients lost capabilities and how it will affect not only the patient and their caregivers, but also society, are steps needed for better research and translation of this devices. On a further note, to correctly address patients' needs is still an ambiguous field. Lots of work has been done in recent years, but more engagement with patients and to fully understand their real needs on the short and long term will improve adoption and, even more important, will improve long-term usage of BCIs.

Reimbursement is hard for neurotechnology devices like BCIs. Often, these are in the research phase and have not been submitted for regulatory bodies making matters more complex. When the research occurs in academia or in research centres linked to universities, there is often a lack of expertise to understand neither the regulation nor the reimbursement process. Collaboration with health economics consultants, for example, is often required. From the companies' point of view, these systematic barriers for health technologies may constitute serious problems, as the time and resources it consumes will make it harder for the company to grow and keep investing in R&D.

A parallel pathway may surge from the wellness industry, mainly in the case of non-invasive BCIs. Even without getting a regulatory approval, there are already direct to consumer devices, presenting an opportunity for companies to generate profit while waiting for medical approval of the devices and the guarantee of reimbursement afterwards. This direct-to-consumer device pathway happened with wearables, so there is the opportunity to learn from that already and balance the pros and cons of this approach.

To have clear guidelines for the use of BCIs as a treatment is also important. This would increase clinicians, therapists and patients trust and would make it easier for the reimbursement process. However, guidelines will depend largely on significant outcomes showed on an extended sample. To develop standards and guidelines for this neurotechnology may sound good, but there is also the danger for it to prejudice somehow the development of BCIs. A more balanced approach might be to have whitepapers and informal guidelines that serve only as a guidance to R&D in the BCI field, improving transparency and knowledge sharing in a comprehensive way.

4.2.2.3. Adoption and implementation perspectives

To define a pathway to clinical adoption also proves to be tricky. Beyond regulatory approval and the need for reimbursement, to understand whether it is going into an hospital or clinic, in getting something implanted or not and getting trained on the device are some of the examples of things to consider when defining a pathway into the healthcare system.

Even if BCIs are approved by regulatory authorities and reimbursed, patients may not feel comfortable and confident using them and that is something that should always be addressed when developing medical devices. At the end, the most important thing is to really know if the patients want and will use BCIs and that is why the must be at the centre of all the technological developments. There must be follow-up processes and long-term monitoring of the use of BCIs, not only to have a continuous assessment of safety in real-world environments, but also to understand if patients keep their engagement and their usage and if there are improvements that will benefit the patients the most.

Adoption by patients is also influenced by the need of training and calibration. These may be long and need high levels of attention, which can result in loss of focus and fatigue. The need for better graphical interfaces and, in some cases, gamification approaches have proven success in getting the patients more motivated and engaged. Better designs and better-looking devices in aesthetic terms is also important. The current complexity of setup of some of these devices is also something to be addressed as this complexity makes BCIs not feasible to an easy use, so to decrease complexity will improve the experience both for patients and for health professionals. To close the gap between the enthusiastic engineering work and real-world scenarios, an understanding of the health ecosystems and the patients' insights will add value and make BCIs have a wider adoption.

Another barrier that may exist, largely depending on the context, involve medical professionals' reluctance to adopt new technologies and to change approaches to disease. In fact, Healthcare systems are known for being slow adopters of technology when compared with other industries.

It is important to note that this comes from the fact that healthcare professionals must be confident of a device safety and real capabilities to have a real use and impact in the patient's life, therefore they are not willing to adopt things they feel have not been enough tested yet.

A participant commented that one major issue regarding the translation of BCIs to clinic is connected to some practical issues when going out of the laboratory into an hospital or a patient's home. This comes with some frustration and demotivates researchers and patients to adopt BCIs. Also of note are the expectations that come with the technology and that may also shape clinicians and patients' adoption if, for example, the device does not live to previous expectations created. The role of media and its influence in society and patients' perceptions are also of note and is discussed ahead in section 4.2.2.5 "Societal perspectives".

4.2.2.4. AI and data perspectives

AI is already useful for detecting error potentials and use them to enhance calibration and adjust the BCI itself to the patient. This is a way to correct and adjust calibration, but it may also have limitations, as this system will be prone to understand and correct errors, but not to reinforce the right use and good learning processes. In this sense, machine learning will be more "willing" to learn from negative reinforcements than from positives, so to use real-world categories and structure learning for AI and machines will be important for the future development of this kind of technology so it becomes more attached to reality.

On the side of Big Data analysis, the complexity of BCIs, a high channel count and noisy data make it obvious that this analysis will require help as otherwise, it will be human impossible to deal with such amounts of untreated data. AI tools already play a role on this theme. Understand hidden patterns on this data and extract meaningful markers from the data obtained from the brain is also a road to explore.

Ethical issues for AI are a hot topic nowadays. With companies having data as business models, there will always be questions about who will own the data, where will it be analysed and how will it be used. Clear understanding and discussion on the ethical issues are needed, but the bottom line is that if data is only being used to improve patient experience and health outcomes, it may be right to access it, always having the guarantee it will not be used to other purposes.

Regarding data privacy, this is already being discussed and it has a great ethical impact, but in theory data obtained from medical devices falls under health data and Europe, for example, has already some initiatives regarding data protection. Although data privacy seems to be an addressed concern, it is not clear who will own the data and to what purposes it may be used. There is the case for companies to own it, so it may be used to continuous development of

further BCIs. On the other hand, there may be interest for hospitals and clinics to have access to it and we should not forget the real owner will always be the patient. Attached to the ownership will always be the question of storing and protecting all the data generated, so this is a complex field and requires further studies from multiple fields to find the best solution.

There is also the legal issue of decision-making. If something fails, who is to blame? The team responsible for the development of AI tools, the hospital, the health system, the doctor? This is also a question when using AI tools for decision-making and in the case of BCIs, there will certainly be some learning to do. On the other hand, the society is also becoming more aware and discussing this thematic, so it may be a question already solved when BCIs achieve clinical settings.

Nonetheless, the impact AI will bring in terms of safety is not to be demised and will probably change the picture in terms of potential to address and met patients' needs with the quality and security demanded by health professionals. Safety contingency mechanisms however are still in preliminary stages and might take time to achieve its dawn.

AI tools will be probably the most decisive tools that neuroscientists will have in the coming years, but this will require them to articulate and coordinate so they can really benefit from technologies. Regulations, guidelines, data privacy are, of course, very important but assuming those issues can be solved, a real culture of communication and collaboration across disciplines will be the way to achieve standardization of the data sharing and data set creation, which will be really what is important to enhance the power of these tools, the knowledge of the brain and the potential of BCIs.

Although most of the opinions regarding the use of AI are positive, sometimes its use may be dangerous and not achieve the desired results. Machine learning and algorithms take time to develop, are largely dependent on high quality data and may not work as intended in a real-world environment. The need to test all the tools in a lab environment, think about what may happen out of it and predict it, along with the responsibility of AI tools, should be cautiously considered during the development of AI tools for BCIs systems, or parts of it.

4.2.2.5. Societal perspectives

Most of BCIs related perceptions are highly influenced by science fiction but, to a higher degree, by social media and media outlets. Often, they picture BCIs as flawless devices, exaggerating their capacities. This overexaggerating makes patients more prone to use it at first but will also lead to frustration and abandonment of BCIs systems as they will not match patients' expectations. Relating with science fiction, this is usually not a positive connection, as devices like BCIs are heavily linked to evil individuals. Great communication skills and a precise discussion about what is possible to achieve with BCIs and what is not possible should be a very important part of the informed consent to use these neurotechnology devices as a form of overcome misrepresentations.

In its core, technology and BCIs are not either good or bad, it will only depend on how humans will use it. Common sense and wisdom should guide our use of technology. It is also important to remind there are no miracles and setbacks are part of the way, but to foresee and try to prevent those more consequential should be a role of all the development team. Technological literacy, both from health professionals and from population, may help deal, raise awareness and lead to a better thinking around all the issues and potentials solutions.

Media have the power to influence society towards their opinion of BCIs towards both negative and positive feelings and representations. They can give more visibility to the field but at the same time also trivialize some of the effort, which is needed to build medical solutions, so there is the need to navigate both the company world and a society world.

Nowadays, BCIs are going through a new phase of hype and propaganda that have bring investment and money needed for the continuous development of these devices but might, in the long run, contribute to send wrong messages and be of prejudice in the long term. One should look it cautiously and be pragmatic about what is possible keeping in mind the risks and benefits in a tailored approach to each patient and avoiding mediatic claims. It is important to understand in which cases there is a real benefit to the patient and ethical values like beneficence, non-maleficence and patient autonomy must be regarded.

Even if some neurotechnology is still in early stages, if benefit for the patient overcome the risks and if patient wants to use it, there should be open minded and participate to achieve a tailored approach for that patient. To be honest and to keep expectations realistic are key factors in a successful media communication.

Ensuring patients own autonomy will require neutrality towards these devices and concise and precise explanations about the pros and cons of these devices in their specific case and probably address some misinformation. Pragmatism and literacy are key in the process of patients' adoption. To have clear and distinct strategies towards the communities BCIs might benefit is mandatory. To involve end users of the intended technology towards all the R&D process is key to be sure to address patients' needs and expectations.

The real-world may also differ from region to region or between countries. When developing BCIs, is important to understand our target countries barriers and to engage with stakeholders that understand that country culture, society and health and research ecosystem.

The look of people towards a disabled person may shift when that disabled person uses technological devices like BCIs and society may associate it to cyborgs. This may lead to new ways of discrimination. On the other hand, a person own view of herself may also change and have impact on how that person looks at herself.

However, we should have in mind generalization is dangerous, especially when there are societies so different around the world. Furthermore, perceptions and technology acceptance also evolve over time.

One topic previously mentioned, entered once again the discussion: direct-to-consumers BCIs. If these devices start to be used by general population there is the chance to gain some reputation if they, for example, improve immersive experiences or relaxation and other wellness related factors. These direct-to-consumer BCIs may be an ally for promoting BCIs, especially the non-invasive ones.

The fear of starting to use devices like BCIs to other purposes like military and human enhancement, with the last one contributing to also deepen social disparities and inequities, is also of note.

4.2.2.6. Parallelisms to other technologies in healthcare

When it comes to medicine, there is a big discrepancy between treatments that are pharmacological and treatments that are non-pharmacological, in which BCIs and technology would fall under. Thinking about the healthcare ecosystem, when developing a treatment with drugs there is clean pathway set up by the regulator in which a certain amount of evidence is required (for example large randomized control trials) The investment to finance all these complex steps of the process is secured by big pharmaceutical companies. Comparatively, when developing technological solutions as a treatment, there is no clear pathway and there is no easy access to financing from large and established companies, so the development of BCI systems will mainly depend on government research grants. Another question is that in the sphere of developing technology, a lot is being done in within the engineering field and there are not a lot of clinical studies done towards BCIs.

To learn from steps already taken by other health industries like pharmaceuticals may help, but there must be the understanding that to want a direct comparison between medical technologies and drugs development may not be the best option.

Drug development has clear guidelines to being approved and reimbursed and, to a certain point, technology may mimic some steps. However, it is clear there are some important differences that need be accounted for, so mimic a process but having in mind the peculiarities may be a way to look at BCI technology adoption in healthcare. Regarding the clinical trials, for example, it is hard to have large cohorts with medical technology and the measured outcomes may be different from what doctors expect from drugs. Also, in medical technologies approaches, frequently a new hypothesis of treatment for conditions that have no current treatment are being tested, so it is not possible to make a direct comparison. All this and the added complexity of BCIs contribute to the fact that studied technologies prove to be hard to reproduce and this may be an obstacle to improve its adoption by health professionals and the healthcare systems.

One parallelism that may bring more information and ideas to improve the pathways for the translation of BCIs to clinical settings are Deep Brain Stimulation (DBS) devices. DBS may show a more similar route for translation of devices like BCIs to the clinic and several participants noted DBS devices have been recently translated to clinical settings. This success of DBS, as a medical device, may paved part of the way for other neurotechnology devices to follow a similar path to achieve translation.

The problem of obtaining sustainable funding for continued research and improvement of BCIs is no different from what happens in commercialization of several technological devices. Not all the devices that have been researched will make it to a commercialization phase and this is a bridge to what also happens in the medical devices field. However, to make the neurotechnology devices more efficient and achieve patients that may benefit for it a more comprehensive and global approach to funding mechanisms might be needed.

As reported regarding other problems of BCIs development and translation, we might be able to learn from previous experiences and Digital Health may paved some of the way regarding AI and data.

Questions related to social and own perception of using a technological device have been frequent over the development of these devices and we may think about the way cochlear implants were first received by society and even patients and the importance these devices hold today to the community that needs them and benefits from theirs use.

4.2.2.7. Summary table of findings

Previously reported findings have been synthetized according to perspectives from participants in Table 8 and 9.

TABLE 8 | Summary table of focus group perspectives (research and healthcare ecosystem)

Research	Healthcare ecosystem
Approximation, share and cooperation between professionals	Impact on patients' QoL is key for reimbursement
Conciliating technological development with medical and clinical outcomes and expectations	Think about specifics of different health systems
Need for a strategic and oriented approach	Maintain cost-effectiveness of the devices
Sustainable and balanced funding for continuous research and improvement as well for breakthrough discoveries	Commitment to clear goals and expectations from all the stakeholders
A platform to bring academia, research centres and enterprises in common ground may help shape future projects	Clear pathway towards regulatory approval and reimbursement

Need for engagement with all stakeholders for research that really meets needs	Always meet patients' needs
Start local and understand the environment	Create evidence for clear clinical guidelines

TABLE 9 | Summary table of focus group perspectives (adoption and implementation, AI and data, societal)

Adoption and implementation	AI and data	Societal
Involve the patients from the beginning of R&D	Improve BCI performance	Keep expectations real
Develop metrics of engagement	Address safety	Raise awareness
Follow-up on patients and monitor use	Consider ethical issues	Pragmatism and literacy towards BCI are needed
Healthcare is a slow adopter of technology	Data privacy	Understand local and cultural characteristics
Practical issues on how to implement clinical pathways for BCIs are still a hurdle	Legal issues	Disabled versus cyborgs

5. Analysis of results

5.1. Potential clinical applications of BCIs in humans

BCIs potential applications to clinical conditions include rehabilitation and restoration, to some extent, of loss functions due to neurological conditions(53). Most of these potential applications fall under conditions that are unmet, at the moment, by current therapeutic options.

Despite their potential applications in healthcare settings, including homecare, BCIs are not yet available to most of the potential patients that might benefit from the use of these devices and remain more or less constricted to research settings(54).

Although BCIs specifications were not in the scope of this work, it is important to differentiate between invasive and non-invasive devices (Table 10). Looking at this table, it may seem like invasive BCIs are the best option, but this is not truth. Surgical procedure and long-term degradation of the device carry serious risks to health and, therefore, the use of invasive devices should be carefully accessed.

TABLE 10 | Comparison of invasive and non-invasive BCI (28,55)

	Invasive BCI	**Non-invasive BCI**
Resolution	+	-
Signal/noise ratio	+	-
Speed	+	-
Accuracy	+	-
Setup	Easier setup	Lengthy setup time
Risks	Surgical procedure and encapsulation in long-term	Not described

The use of "+" and "-" is just symbolic and intends to mean one is better when compared to the other.

Each type of BCI will have its own specific set of advantages and disadvantages, but for input modalities that are currently under development, technologies that are less invasive tend to be more limited in their potential speed, accuracy, usability, and generalizability(55).

Most studied conditions, include individuals with chronic paralysis from multiple causes, including SCI, spinocerebellar degeneration, ALS and stroke(53).

Some of these conditions (TBI, ALS, brainstem stroke) may result in LIS and, due to the impairments this condition brings to patients, this is a condition where patients and their families seem to have a large acceptance of the use of these devices, resulting in several studies of BCIs application to LIS. Better results in LIS patients have been achieved when using invasive devices and it seems in the future the tendency is to continue to study and use invasive devices for people with LIS. Nonetheless, little evidence has been gathered so far to support applicability and efficacy of BCIs for TBI in a clinical setting(62).

For motor recovery after SCI, evidence for the efficacy of BCI-augmented therapy is also preliminary(53). On the other hand, the stroke literature for functional restoration through BCI-augmented therapy is more robust(53). This literature is more focused on the use of non-invasive BCIs in therapeutic plans for neurorehabilitation for the upper limp. There is less evidence supporting lower limb applications to stroke patients.

Other applications of BCIs are still in a very early stage of research.

A division of the potential clinical applications of BCIs in humans, according to its maturation level, is proposed. This division is the result of perception, literature research (see section 4.1 "Summary of systematic review findings: potential clinical applications of BCIs in humans" and Appendix 2) and subjective analysis and comprises three stages: strong clinical evidence, moderate clinical evidence/ongoing clinical experimentation and early stages experimentation/promising basic research (Table 11).

TABLE 11 | Potential clinical applications of BCIs in humans according to level of evidence

	Clinical application	**Type of BCI**
Strong clinical evidence	Upper limb neurorehabilitation in stroke	non-invasive
Moderate clinical evidence/ongoing clinical experimentation	Lower limb neurorehabilitation in stroke	non-invasive
	Control of assistive devices in LIS	invasive
Early stages experimentation/promising basic research	Sensory Restoration in stroke	non-invasive
	Phantom-limb pain in amputees	non-invasive
	Motor recovery after SCI	invasive
	Cognitive training in ADHD	non-invasive
	Therapy in TBI	non-invasive
	Glaucoma diagnostic	non-invasive

5.2. Barriers and opportunities to wider clinical adoption

In terms of technology, BCIs seem to have achieved a state where they are safe and reliable to use. Besides, they may offer a solution to address clinical needs that are currently unmet. Still, there is the need for more studies to expand knowledge about brain and its mechanisms, as well as to guarantee the applicability of BCIs to clinical conditions.

The heterogeneity of patients and lack of patients' characterization in the studies led to a difficulty in identifying the ones that might benefit the most from these devices. Sample sizes of the current studies also fail to give confidence in a generalization of outcomes to a particular population.

Health professionals may play a role in understanding and conciliate objectives from the engineering and clinical side of research, enhancing trials design to evaluate relevant outcomes for the patients. Fulfil the diverse goals of a multidisciplinary team and understand how to integrate engineering improvements into clinical benefits is still a challenge.

Although the human brain and its mechanisms are not well known, this knowledge has been evolving and if BCIs prove to be feasible, safe, reliable and clinically beneficial there is the case for its adoption even if not all mechanisms are understood to the current science. For health professionals, to accept these unknown mechanisms might be harder, but in healthcare practice there are drugs being used with good results and without a well-known mechanism, which may be a reminder that not all the interventions have that background knowledge supporting its use.

There is still the need for more research, however a strategy in place to guide research towards relevant goals for healthcare in a larger extent and to patients is needed.

Continuous funding from R&D of BCIs to translation into clinical practice may also be a hurdle, but the picture of funding is changing and may bring the resolution for some practical issues. Public funding to help translation, partnerships between public and private sector are initiatives that may help close the gap in manufacturing innovation.

Platforms that join academia, research centres and enterprises in collaborative projects may work as a catalyst to the development of multidisciplinary work relationships.

Regarding the regulatory and reimbursement processes of health systems, these are unknow to some extent for some of the participants and it was a harder topic to comment on. Nonetheless, most of the participants feel there is the need for an easier and simplified process to navigate through regulation and reimbursement.

Although regulatory bodies are perceived as conservative, to include them as stakeholders and actively engage with these institutions to better understand needs for approval and find key points of device characteristics is needed. It seems the most important features to be met are

safety and stability of the device. To think about BCI as a modular system, comprised by hardware and software and with multiple components, approaching the regulatory needs in a progressive way and adding on components in different timelines may enhance pre-approvals and make a simpler device ready for market while testing and funding one with larger and different capabilities.

Fast-track programs that include regulatory and reimbursement approval for initial stages of BCIs may help bringing them to the healthcare market while proving their long-term benefits. However, for this to happen there is the need for the device to prove safety and a clinically relevant outcome before approval for fast-track. Patients may have a crucial role in engaging and bring together the remaining stakeholders in a larger platform to discuss the better way of approaching this issue. It is important to remind that if BCIs prove in initial stages their benefit to patients, patients and their families and caregivers will be more eager to lead initiatives like this one.

On prospects of software development for BCIs, the role of AI raises some questions. Algorithms may have a role in controlling applications or end effectors, but the use of machine learning to analyse brain signals must account for ethical issues that may arise with the use of brain data.

Thinking about function and outcomes from the therapeutic use of BCIs, while reflecting about its cost is crucial. For BCIs to be accepted and, mostly, to achieve reimbursement, it is important to keep things real and understand when technological improvements that may be expensive really translate into significant better outcomes. This has a direct connection to cost-effectiveness of the BCI intervention and may condition approval.

A commitment to and between all the stakeholders, to make sure clear goals and expectations are in place and to define a clear pathway towards regulatory approval and reimbursement from the beginning will be a catalyst for successful implementation of BCIs towards widespread clinical adoption.

Regulatory approval and reimbursement are important steps, but adoption by patients and healthcare professionals is one of the most determinant aspects of a successful implementation of BCI interventions. Follow-up processes and long-term monitoring of the use of BCIs will be needed to continuous assess safety in real-world environments, but also to understand if patients keep engagement and usage of BCI as well as understand real benefits.

Practical issues on how to implement clinical pathways for BCIs, deciding when to use them and when there are better alternatives, how to integrate BCIs in a healthcare facility or even at a patient's home still needs thinking and creation.

The role of society in large-scale adoption of this kind of technology is also discussable. It will always depend on the context and current perceptions and preconcepts of each region.

A change of paradigm from science fiction is already occurring, but it is important to not get into a hype where expectations are set too high to be achievable.

Understand real-world scenarios and characteristics, with cultural and local differences is an issue that needs to be considered when thinking about scale-up adoption.

Manage expectations and keeping clear expectations about what is possible, without getting in science fiction or in exaggerated claims while maintaining a discussion open will require great communication skills. BCIs are easy to catch attention and society perceptions will be easy to be influenced, so false steps may have implications on the long run.

A reflection of aesthetics of the device is also important as minor improvement may influence patients' adoption and society perceptions. Direct-to-consumer BCI have a great focus on design and patients will expect that of BCI as medical devices. The look of the device and how it looks on the patient have an impact on adoption. Even invasive BCIs are somehow visible, so it is important to address this topic and improve not only awareness of BCIs, but also to keep them as enjoyable to the eye as possible.

Still regarding direct-to-consumer BCIs, they may serve as a basis for financing medical research and may even have a positive impact on society perceptions and preconcepts of technological devices. However, it is important to understand these devices do not have the needs and restrictions of medical devices and may also undermine public trust and confidence on BCIs. Literacy, managing the hype and engage with all stakeholders to improve trust around technological devices for medical use, understanding points of difference from direct-to-consumer devices is important.

When thinking about technological interventions in healthcare to have some comparison and learn from previous lessons may be useful. It is important to understand although these parallelisms may serve as a guidance, each technology and intervention has its specificities that should be studied and addressed.

Drug development pathway from research towards widespread adoption may give hints about steps to follow, however BCI is very different from drugs. Nonetheless there is always the need for evidence, proof of safety and significant improved outcomes.

More recently, DBS devices have also been approved as a medical device and they may provide a valuable lesson for technology interventions to achieve widespread adoption within the health system.

Regarding concerns about AI and data, current growth of digital health solutions has improved public knowledge and concerns, leading to clear recommendations and guidelines from researchers, public institutions and governments on how to address current concerns. A larger governance on health data and AI in health is expected with the growth of digital solutions in healthcare.

In the past, concerns about the use of technology to address clinical needs have also been discussed in society. When the first cochlear implants entered the healthcare market there was quite restraint from public to its usage. However, societies evolve and its own perceptions and preconcepts are always an unfinished process.

Main findings regarding barriers and opportunities to widespread clinical adoption of BCIs are summarized in Table 12.

TABLE 12 | Summary of barriers and opportunities to widespread clinical adoption of BCIs

	Barriers	**Opportunities**
Research	Heterogeneity of patients Poor report of technology and patients' characteristics	Improve partnership between technological and clinical fields Develop standards, guidelines or whitepapers to report BCIs interventions
Funding	Public funding focus on ground-breaking advances Gap to translation funding	Reduce the gap between initial funding for new and innovative technologies and the funding for translation Improve public-private partnerships to address this funding gap
Regulation	Not innovation friendly Lack of clear regulatory and legal paths	Improve dialogue and partnership between all the stakeholders Fast-tracks and clear guidelines
Reimbursement	Not guaranteed	Create a parallel and continuous pathway from regulatory approval towards reimbursement
Adoption	Lack of trust	Improve technological literacy Raise awareness and build trust

5.3. Contributions to Health Policy implications

To bring neurotechnology to a heavy regulated market, like the case of healthcare, takes time, investment and a real push from multiple stakeholders to achieve the possibility of success.

A collaborative environment from all the stages of R&D of BCIs in healthcare contexts is needed to improve the chance of making these devices available for every patient in need.

The need for integration of different areas of knowledge and to improve technological literacy may not only add something to the field, but also to the current picture of healthcare, contributing for new views and approaches that may result in several improvements in the health system. Nonetheless, healthcare is considered to be conservative and slow in adopting changes, so strong evidence for clinical use will play a significant role in widespread adoption of BCIs.

When thinking about the translation of BCIs into widespread adoption in clinical settings it is important to take in consideration the continuous investment to fund research and improvement of the device, as well as understand how healthcare professionals and patients will react differently to the innovation in the specific context of implementation.

Nowadays there is not a clear pathway or a use case of how to implement BCIs in healthcare practice, but to connect with patients and healthcare professionals might be the first step in developing this case, which can be adaptable over the time with learned lessons.

Guidelines, standards, or whitepapers to comprehensively report BCIs interventions and respective outcomes are crucial to better structured evidence.

Aggregate public funding with private initiatives in a partnership for the translation and continuous improvement of neurotechnology devices may be an option in bringing neurotechnology devices to patients, scaling up and making it wide available and work as a catalyst to the development of multidisciplinary work relationships.

In this context, the strategy may start at a local level, where local infrastructures already have the knowledge of their specific environment and needs and based on that experience, start to scale-up and introduce the necessary changes learned from the experience.

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6. Discussion

6.1. Potential clinical applications of BCIs in humans

BCIs have shown potential, to some extent, to be a therapeutic option to specific groups of patients, achieving current unmet clinical needs.

On some medical conditions, feasibility studies and clinical trials have been conducted showing the potential is real and more research may lead to an integration of BCIs as a therapeutic or diagnostic tool in healthcare.

Addressing the clinical applications envisioned in this work as those with more evidence (see Table 11 in section 5.1), neurorehabilitation after stroke with non-invasive BCI and the control of assistive devices with an invasive BCI seem, at the moment, to be the most promising clinical applications.

In fact, the use of non-invasive BCI as a neurorehabilitation tool for stroke patients has already been approved by the FDA(70). This was achieved through a De Novo classification(71) available for low to moderate-risk breakthrough devices and means this BCI has proven safety and effectiveness as a upper extremity rehabilitation device for stroke patients.

Neurorehabilitation therapies with BCIs in stroke patients may integrate healthcare pathways as a complement of interventions like physical therapy and its price, combined with the possibility of being used for multiple patients together with low risk makes non-invasive devices closer to widespread clinical adoption.

Non-invasive clinical BCIs, already FDA approved, may provide a steppingstone to invasive BCIs and will be important for those users who do not qualify for (or do not prefer) invasive BCIs. However, FDA approval does not mean these devices will be available for reimbursement.

Invasive devices, due to its higher risks, have been tested only in patients with serious disabilities and therefore the evidence generated include conditions like LIS. In this population, BCI have shown potential to help patients to communicate and improve their autonomy in activities of daily living (ADL).

It is important to note that usually patients with chronic severe disabilities have happiness levels matched to the general population and they accept their condition. There might be the case of patients who do not want to go to surgery to implant a BCI and patient autonomy is to be respected. This factor combined with the high cost of invasive BCIs make invasive solutions harder to adopt. Despite these challenges, the advantages invasive BCIs (see Table 10 in section 5.1) bring to their user must be considered, principally when in long-term usage.

To any potential clinical application of BCI there should be a case of use based on evidence, integration and implementation in healthcare system, cost and need of the intervention. This should be complemented with a benefit assessment and an informed consent to the patient and/or caregivers, giving an honest overview and respect autonomy.

In the long-term, the introduction of BCI interventions ask for a way to collect data on its safety and effectiveness during real-world application. This may enable a better understanding of the brain mechanisms and of the real impact BCIs may have on patients QoL. As any technological intervention on healthcare, data on BCI engagement and usage from patients in their real live will help to better address patients' needs and continuously improve BCI according to the patient needs and preferences.

The big promise and interest surging in BCIs, that have shown promise in some clinical areas, is still to live to its hype and acquire scale in healthcare.

6.2. Barriers and opportunities to wider clinical adoption

Technical challenges in non-invasive BCIS comprise data acquisition, signal processing and classification, end-effector device, priming and feedback environment and integration of these four elements(5). The nature of these challenges means that a multidisciplinary approach is required and it seems probable that progress will be made by different laboratories tackling some or all of these elements and coordinating information sharing and technology improvements(5). Once the challenges have been met, robust clinical trials can be conducted to ensure that the promise of this approach does translate into solid empirical evidence supporting the use of these systems within clinical settings(5).

Despite its surgical and implantation risks, the future of invasive BCIs seems bright. Several studies already demonstrated that the implanted device retain functionality for more than 1,000 days after implant, while enabling highest BCI performance so far, compared to non-invasive technologies, for restoring communication, arm control, and general-purpose computer use(60,72).

There is also significant improvement in these invasive devices, with a study already reporting the first use of a wireless BCI in human subjects, at home(9). This study demonstrated the viability of a wireless BCI, highly comparable to wired devices, enabling ongoing fundamental research into cortical processing during every day human behaviour to inform future neuroscience and BCI advancements(9). More important, this is a step to overcome several former barriers to in-home mobile independent use of a promising assistive technology to restore communication and digital access for individuals with severe speech and/or motor impairments(9). However, it is important to remember that with portability new problems may emerge like, for example, power delivery.

Technical challenges, cost and safety for patients to use BCIs on their own seem to be addressable issues at the time.

Current initiatives by IEEE Brain on a roadmap for standards for BCI and recommendation from OECD are already addressing some of these issues(15,44).

On the field of research, studies seem to become more complete, detailed and with an orientation towards clinical application. A major factor in this emerging field is the long-term safety of a permanently implanted BCI device in the brain. To assess efficacy outcomes and to pivot first trials are steps to seek the first approval for a BCI that can be commercialized as a medical device.

Currently, science funding is based on a linear model where public funds are often distributed for basic science research, leaving applied science and development as well as translational science to be funded by the industry.

There are already initiatives to change and accelerate translational sciences pipeline, aiming for a quicker move from basic research to its applications, and enhancing social benefits. However, a balance will always be needed and solid results between translation of BCIs into real-world settings applied to Medicine will always be needed to make sure they are safe, bring real benefit and have a bigger chance of patient's adoption.

Approaches for quantifying QoL are also being addressed and reported, with a particular interest in quantifying QoL of technology interventions, which in the future can lead to a better perception of the impact of technology in the life of the patient and its social context(73).

The term AI is misunderstood not only by the public but also by technologists and there is the need to better understand the term and what it means(74). Computers have not become intelligent *per se*, but they have provided capabilities that augment human intelligence(74).

AI and machine learning can serve to augment and enhance some characteristics of BCI, via painstaking analysis of large data(74). Machine learning also can provide new by bringing together information found in multiple data sets, finding patterns, and proposing new courses of action(74).

However, for the foreseeable future, computers will not be able to match humans in their ability to reason abstractly about real-world situations, there will need well-thought-out interactions of humans and computers to solve most of the problems(74). There is the need to understand that the intelligent behaviour of large-scale systems arises as much from the interactions among agents as from the intelligence of individual agents.

When it comes to data security in health, it is important to remember several countries already have policies for data governance, like for example the EU GDPR and USA HIPAA, so this might not come as a barrier when it comes to BCI widespread adoption in clinical settings.

A modular BCI may be a solution to mitigate and integrate several problems. Thinking about a BCI as a part of the system where hardware for signal acquisition and software for signal processing are integrated as an operating system that may be connected to several applications or end effectors (see Figure 2 in section 2.1.1) may improve the range of solutions, the way AI is integrated in BCI systems and even be more favourable to regulatory approval. This way, regulation would work in steps being the first to approve the signal hardware and software, which will be the "proper" BCI, and after approving each end effector or application to the intended use. However, regulators probably will not change its policies easily either and they will be probably committed to the current consensus.

Modularity platforms may also accelerate the innovation of subcomponents and promote collaboration(75). These platforms could also enable new business models to help coordinate research activities and to increase translational efficiency(75).

Another way to approach regulation is to create a spirit of collaboration and engagement with all the stakeholders. In this point, patients' communities play a key role as they may function as a catalyst to approach regulator to the other stakeholders, favouring communication and engage in new ways of thinking policy for patients that are eager to look for solutions for their conditions.

Medical associations also may have a role, as it is common for clinical guidelines and guidance to be published by this associations. To include technological interventions that proved value in these guidelines may improve clinicians' awareness of devices like BCIs and when to recommend their use. This does not mean that guidelines will automatically recommend BCI interventions, instead they can recommend or not their use based on class of recommendation and level of evidence.

The likelihood that BCI systems will be adopted in clinical practice calls for reimbursement planning and, thus, for a relevant role for policy makers such as insurance companies and/or health care systems(58). The prerequisite step to address this factor in BCI transferability is represented by the industrial take-up of research products(58). Technology-supported interventions such as BCI aim to reduce the costs of rehabilitation by optimizing the ratio between a successful rehabilitation outcome and the required (human) resources to be involved(58). Home-based rehabilitation in this sense represents an attractive perspective of future BCI-based interventions(58).

The acceptability of society towards BCI is likely to evolve towards the time. Current interest and hype may change the look and preconcepts of this kind of devices. Direct-to-consumer

devices are also likely to function as an enabler towards acceptance. On the other hand, it is very important to keep expectations real and not let expectations go above the real capability of BCIs.

To manage expectations versus reality for patients as they may search the internet or find media cover of the most advanced BCIs, which are not suitable or tested for most users.

A BCI for healthcare use should be tailored to the patient, to the society and to the health system itself. Not create a barrier to access, improve patient QoL, autonomy, maximize health benefits and minimise risks are key in developing BCI interventions. When developing BCIs and neurotechnology devices, matching the wishes and needs of the user is the most important.

Several barriers and opportunities to wider clinical adoption of BCI are closely related to other technologies adoption in healthcare systems and have a relation to health policy (Figures 15 and 16).

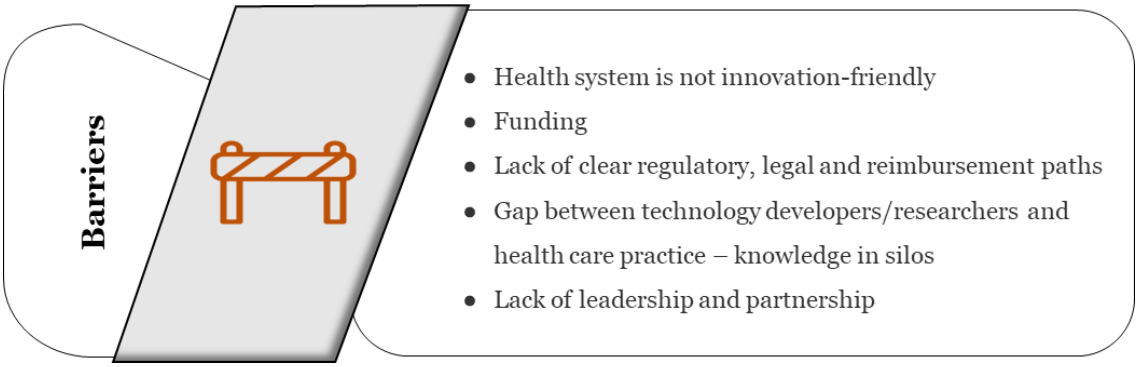


FIGURE 15 | Barriers to wider clinical adoption

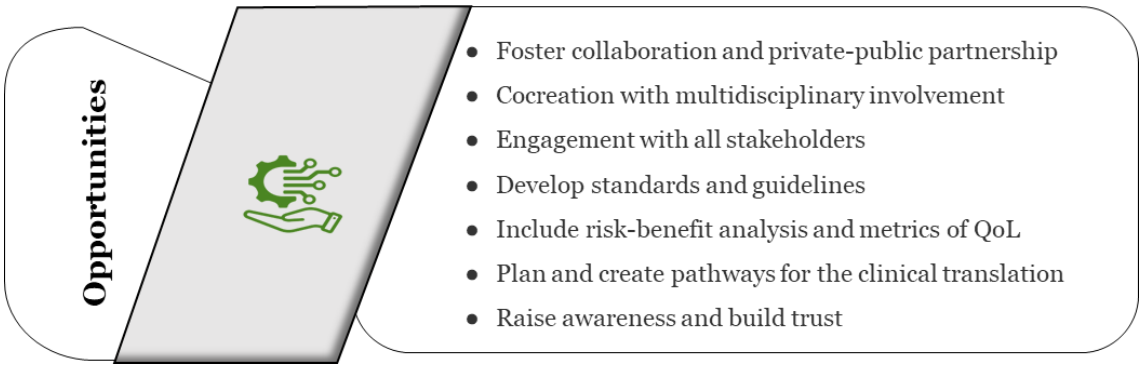


FIGURE 16 | Opportunities to wider clinical adoption

6.3. Contributions to Health Policy implications

While BCI may be hyped as an alternative for some conditions, the reality is that the translation timelines for medical devices and their success rates as therapeutic tools are slow and costly rather than mirroring the lean, accelerated development of technological devices for the direct-to-consumer market(75).

The intrinsic complexity of healthcare systems may lead to duplication of efforts, inadequate use of scarce time and resources and confusion and conflicts, if decisions are not well aligned or in the absence of broad coordination(39).

Bringing a BCI to market will entail transforming a bespoke technology, bed-tested in a small number of patients, into a medical device that can be manufactured, implanted (in the case of invasive BCIs) and used at scale. Large trials need to show that BCIs can work in non-research settings and demonstrably improve the everyday lives of users and at prices that the healthcare market can support.

Future progess will depend on the recognition that BCIs bring multiple players to the table, and their development, implementation and scale up in the health ecosystem will require inter and multisciplinary efforts to be achieved(4). Patient is the centre of patient centred approach in medical sciences and user design in technology.

A framework embodying clinically relevant outcomes for patients and HTAs of the BCI technology used would be useful for a better division of the BCIs' clinical applications that have better evidence of being closer to a translation into healthcare practices. This division should include clear information and indications regarding the condition to be addressed as well as potential risks and expected benefits.

To achieve such framework requires a coordinated multidisciplinary action plan and may contribute to a better overall comprehension of BCIs interventions in clinical conditions. In my opinion, this may be a small step, but will always be a step towards the creation of clinical guidelines and future integration of this neurotechnology in the health systems leading to a wide clinical adoption. This is a kind of mission-oriented research, which need collaboration with end users to enhance the device and is conducted with promises of use and importance to be achieved.

When addressing clinical necessity, engineers should work with clinicians to identify a common "technology stack" that may serve multiple purposes and establish scientific validity(75). To work in a platform of collaboration can flexibly facilitate clinical investigations with marginal investment.

A well-designed and well-governed platform ecosystem can significantly lower such barriers to translation(75). Innovators should therefore consider how neurotechnology platforms might be designed to benefit from the tailwinds of consumer technology and government research investment while addressing the key barriers that clinical neuroscience and medical device translation face(75).

This ecosystem should fit the Health System itself and adapt towards patients' needs. To understand particularities of the system itself as well as local and cultural significances will ensure better acceptance and adoption.

BCI should be developed to be safe reliable and effective. To fit as the best solution to the clinical condition presented and to be as tailored as possible to the patient, balancing risks and benefits will help clinical translation.

Looking ahead, a range of opportunities where BCIs may provide significant health, societal, and economic value speak to the long-term potential of the field. Nowadays, many of these applications are still in the pre-clinical, experimental, or theoretical stage, and the field will need to overcome significant challenges to achieve widespread, real-world impact.

To be aware of future trends and start to prepare the field early, for a better innovation adoption and enable technologies like BCIs in healthcare, or at least provide a chance to generate evidence about clinical outcomes must be looked for the future of health policy.

To plan BCI interventions, engage with all the stakeholders and learn from their opinions and insights, pilot testing ideas, evaluate relevant outcomes, improve on the generated knowledge and finally implement a valuable intervention is an idea on how the health systems may look to technological interventions in healthcare (Figure 17). This should be looked as an always evolving cycle, that may take steps back in order to improve and learn and can be stopped at any time, for example if stakeholders do not think it will have clinical value, if outcomes show no benefit, etc.

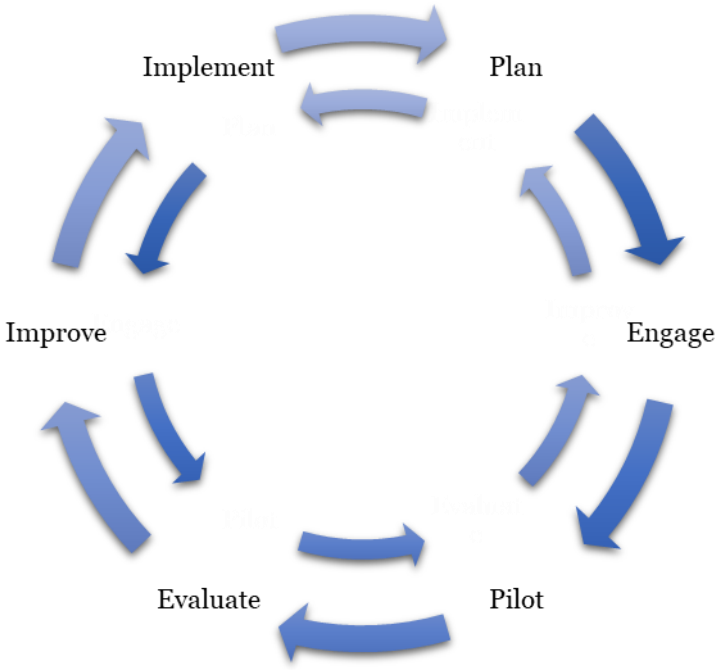


FIGURE 17 | Cycle for technology interventions in healthcare

Currently, many national guideline developers are taking a population perspective when considering health interventions(39). It is important to understand that in the case of BCI a population perspective may not be beneficial, but when applied to a small patients group it show benefits and may be considered as a positive intervention for that group. To include these groups in guidelines should be considered along with larger population perspectives.

To navigate health policy for BCI interventions claims for a multidisciplinary view that spawn boundaries of fields like medicine and technology. Current direct-to-consumer devices and the rise of the so called metaverse are raising awareness for technological devices within the society and to find connections between all the considerations to develop BCIs in healthcare are starting to surge in organizations like The WEF (Annex 5).

6.4. Health innovation

Altought BCIs have already reached diret-to-consumer market, it is important that as a technology to be used in healthcare setting – medtech – there will be more needs and more lens to look at it when thinking about all the R&D stages as well its translation. In healhtcare a new idea, any real innovation, will be difficult to convince doctors and patients to accept. People want and need security and reliability.

Real innovation means companies will need to be willing to fail and lose money. In the case of BCIs, small MedTech companies may go bankrupt if they fail, needing funding and partnership with governmental bodies and agencies to be able to finance some innovative technology.

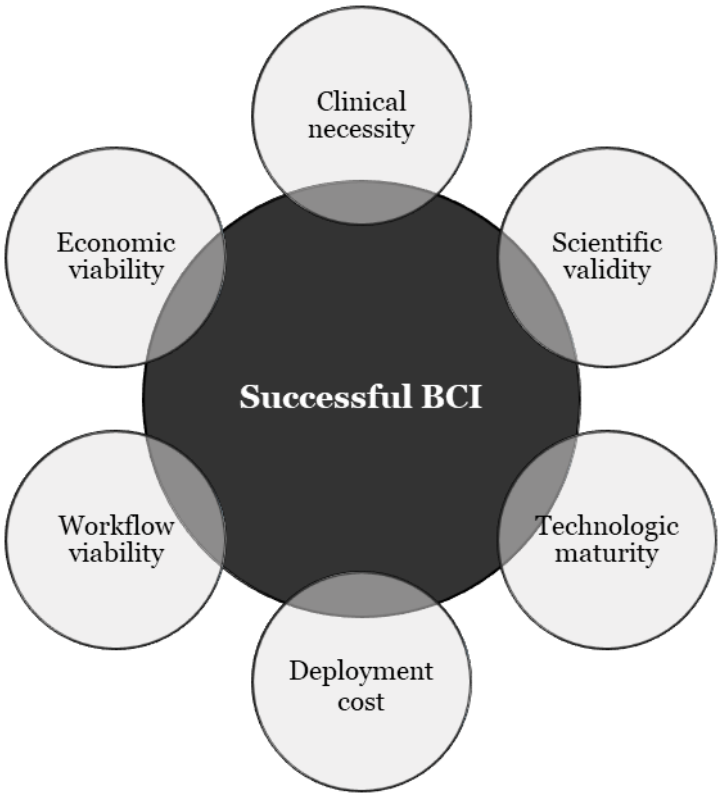
Liability issues or the generally missing innovation-friendliness in the health care system together with missing funding or reimbursement can be factors to implementation failures of technology in healthcare contexts(38).

Successful implementation of technology also depends on negotiating the changes this requires to staff activities and adapting implementation to the wider organisational and social context(35).

Two major gaps to get over and adopt new technologies. The first valley of death is the translational and it is about market forces in the translation of technology to the clinic (typically first in human or small studies already seen with BCIs), which is also known as research to industry (Annex 3)(12). The second includes clinical adoption and market forces to be able to commercialize the device and is correlated with TALC (Annex 2)(17).

To ensure a successful adoption of BCI in widespread clinical settings some factors should be taken into account (Figure 18). These factors include: a clinical problem that is currently inadequately met by existing therapies; a mechanism of action used to identify patient subgroups that would most benefit from the technology; technology which can safely and reliably interact with the body; the cost to bring a medical technology to the marketplace

including the ability to secure intellectual property, satisfy regulatory constraints, and distribute to physicians and patients; ability for the technology to satisfy relevant clinical and patient stakeholders without prohibitive adjustments or burden; and a clear value proposition for the technology that demonstrates economic value to the healthcare continuum(17,75).



Adapted from Pulliam CL, Stanslaski SR, Denison TJ. 2020) (17)

FIGURE 18 | Practical translation constraints for a successful BCI

Innovation in health must address a clinical problem, ensure there is the need, secure funding to solve the problem, ensure the solution will not create new problems, think about the change and time to change and engage with end users to better understand reality.

6.5. Summary table of means to overcome barriers in BCI adoption

A summary of challenges and barriers to BCI widespread clinical adoption and potential opportunities and enablers reported during this work is presented in Table 13.

TABLE 13 | Summary of means to overcome barriers in BCI adoption

	CHALLENGES/BARRIERS	OPPORTUNITIES/ENABLERS
INNOVATION CHARACTERISTICS AND PROCESS	High pace of technology improvement Lack of involvement from healthcare professionals in the process of technology development	Balance novelty with approaches to improve aspects of current available technology Involve healthcare in the R&D, through partnerships that improve technology knowledge and create a common language between all the parts involved Improve user design and patient-centricity Develop and use standards and guidelines Interoperability may help further developments and interaction with current technologies
METHODOLOGY	Hard to compare with other interventions No standard methodology or plan for research Lack of information (from the patients that went clinical trials and from the technology itself)	Understand BCIs are an option for current unmet clinical needs and create a flexible approach to make these devices available for the needed Research with metrics of QoL Include risk-benefit analysis Apply ethical principles Listen to end users in all the steps of R&D
FUNDING	Missing funding	Reduce the gap between initial funding for new and innovative technologies and the funding for translation Improve public-private partnerships to address this funding gap

REGULATION	Health system is not innovation-friendly Lack of clear regulatory and legal paths	New regulations supporting innovative devices (for example FDA Breakthrough Devices Program) Improve dialogue with healthcare stakeholders to understand the needs
REIMBURSEMENT	Reimbursement is not guaranteed	Create a parallel path to regulation to understand what is needed to guarantee reimbursement and improve the pathway
PLANNING	Most research is focused on new approaches and technological novelties	Create a plan to translate the research to the clinic
LEADERSHIP AND PARTNERSHIP	Gap between technology developers/researchers and health care practice – knowledge in silos	Partnership and multidisciplinary cocreation between academia, industry, government, and other stakeholders (patients, caregivers, etc) to facilitate policy-relevant research and increase scale-up – stakeholders' engagement Clear ideas for the pathway for clinical translation
SOCIETY	Lack of trust in these devices Associations with science-fiction	Improve technological literacy Recommendation of these devices from doctors to patients Raise awareness and build trust Need for a cultural shift Have in mind the individual characteristics

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7. Limitations and future work

Due to purposive sampling and low number of participants, views expressed in the focus group were biased towards a positive view of BCIs, however the aim was not to use these groups to discuss a pro vs cons debate, but more importantly, accepting a positive bias, what are the barriers and opportunities for adoption.

This study is exploratory and to my knowledge no similar approaches to understanding barriers and opportunities for the widespread clinical adoption of BCIs is known.

As this study was conducted by a student of Medicine, there is the possibility to bias from a healthcare perspective regarding the interpretation of results and discussions held.

Findings of the systematic review should be interpreted with caution. Due to study design and purpose of the review no generalisations on the use of these devices on particular medical conditions can be made.

The creation of guidelines (eventually a structured data capturing instrument) and a common taxonomy to report findings, outcomes to be measured and other important considerations for research involving BCI is also needed.

The inclusion of more stakeholders and to include other health professionals and other professions may be helpful for getting new ideas into the future of BCIs.

In the future, a workshop with more participants and from various backgrounds is suggested to better understand and add-on on the work presented here. This workshop is to be held during several days, or to be divided in several ones, targeting a barrier at a time and produce solutions to overcome it. This initiative should end in a white paper or even in a framework to develop technological innovations and BCIs within the health systems.

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8. Recommendations

To tackle barriers to widespread clinical adoption of BCIs and catalyse opportunities across the healthcare ecosystem is mandatory to implement a culture of innovation and achieve fast deployment of BCIs in clinical settings.

The most important outcome is to show benefit for potential users. An agreement on health outcome definitions and measurement is needed for better comprehension of multiple interventions. This comprehension will also be enhanced by an agreement on standardised approaches to presenting information and on criteria that are linked to context and recognise that they are overlapping and could require emphasis depending on the decision-making actor and perspective.

To outside own research, be open to collaborate with different players and stakeholders and build bridges with other sciences to grapple with multi and interdisciplinary issues. Researchers may also agree on key domains for rating the certainty of evidence for intervention effects and other criteria that determine decision making. Collaboration may also lead to a platform for modular BCIs where there is hardware and operating system as software, but with the possibility to interoperate with other software, like apps, or other end effectors.

Technological improvements should be focused on accuracy, speed, and usability, both of hardware and software.

Tackle funding inequities and innovative partnerships between public and private entities may close the gap of a continuous improvement of BCI.

Regulators need embrace fast innovation and reduce bureaucracy.

To raise awareness and analyse the health system landscape from multiple stakeholders' perspectives explaining opportunities and addressing concerns about potential challenges may result in interest, generating and enthusiasm and leading to action from the healthcare professionals into BCI adoption.

Consulting with organizations that aggregate knowledge and experience, aim to foster research and advocate for an ethical advance of the field, for example BCI Society and Neurotech Network may provide a bigger picture since the beginning of the process(76,77).

Regarding the three distinct scientific areas focused on this work, three priorities are defined in 3x3 model (Figure 18). From our point of view Engineering should prioritise security, reliability and usability of BCIs when developing them; Medicine should think about be patient-centered, have a tailored approach to each case and never forget ethical values like beneficience and non-maleficience by managing risks and ensure clinical benefits; for Management the priorities should lie in integration of this technology into healthcare pathways, foster collaboration both between multidisciplinary areas of science but also engaging and collaborate with other stakeholders and have a continuous improvement plan.

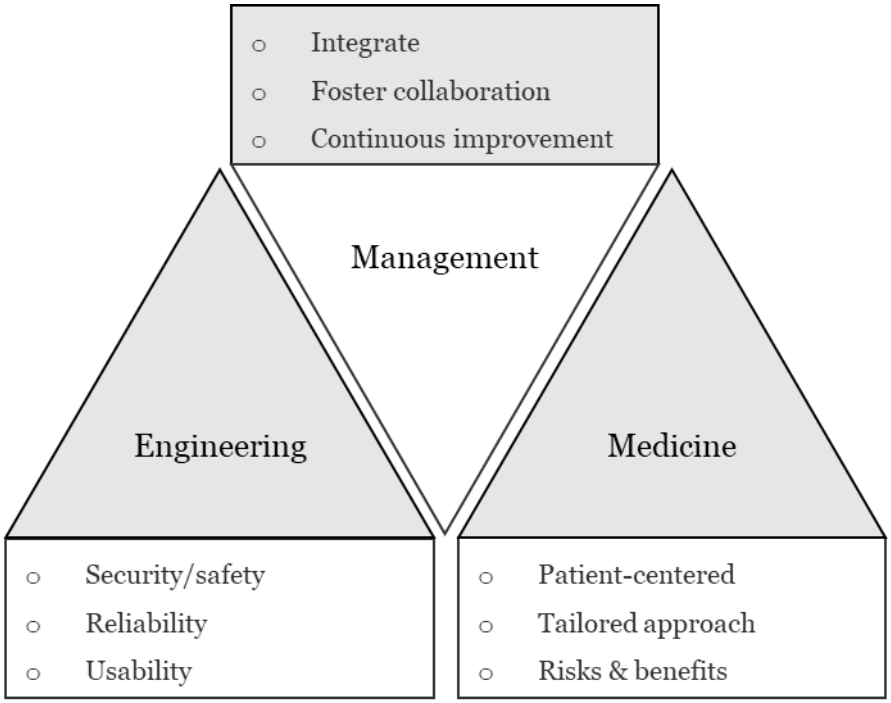

FIGURE 19 | 3 priorities for the 3 areas we focused our work on (3x3) for development and translation of BCIs into healthcare

9. Conclusions

BCIs seem to be at a turning point. In recent years research has been raising the bar and its potentialities for clinical use seem stronger. A new phase of hype and even adoption of BCIs as a direct-to-consumer device may help BCIs stepping out of the lab-bench and successfully achieve widespread clinical adoption.

Promising trials and positive outcomes with relevance for the patients are laying the foundation. Besides technological developments and results showed in research contexts, their translation in healthcare is still lagging.

Some barriers to their adoption seem already addressable, however barriers linked to the healthcare system itself call for a collaborative and coordinated approach, linking efforts to overcome systemic challenges and create opportunities for the widespread clinical use of BCI as a medical device. The translation of BCIs into clinical practice calls for a concerted action and a true partnership between private and public institutions that fosters collaboration and integration of all perspectives and needs.

When (and if) BCIs reach the clinical practice and if clinicians will readily accept these changes and prescribe the devices also remains to be seen. The integration of medical doctors in the teams developing BCIs may bring some confidence to other clinicians, but other initiatives to raise awareness and knowledge of this devices as well as its integration in clinical guidelines may push further its adoption.

This adoption will not depend on clinicians. To engage with a wide variety of stakeholders, understand their perspectives and win confidence and support will help to guide progress for the use of BCIs in healthcare contexts.

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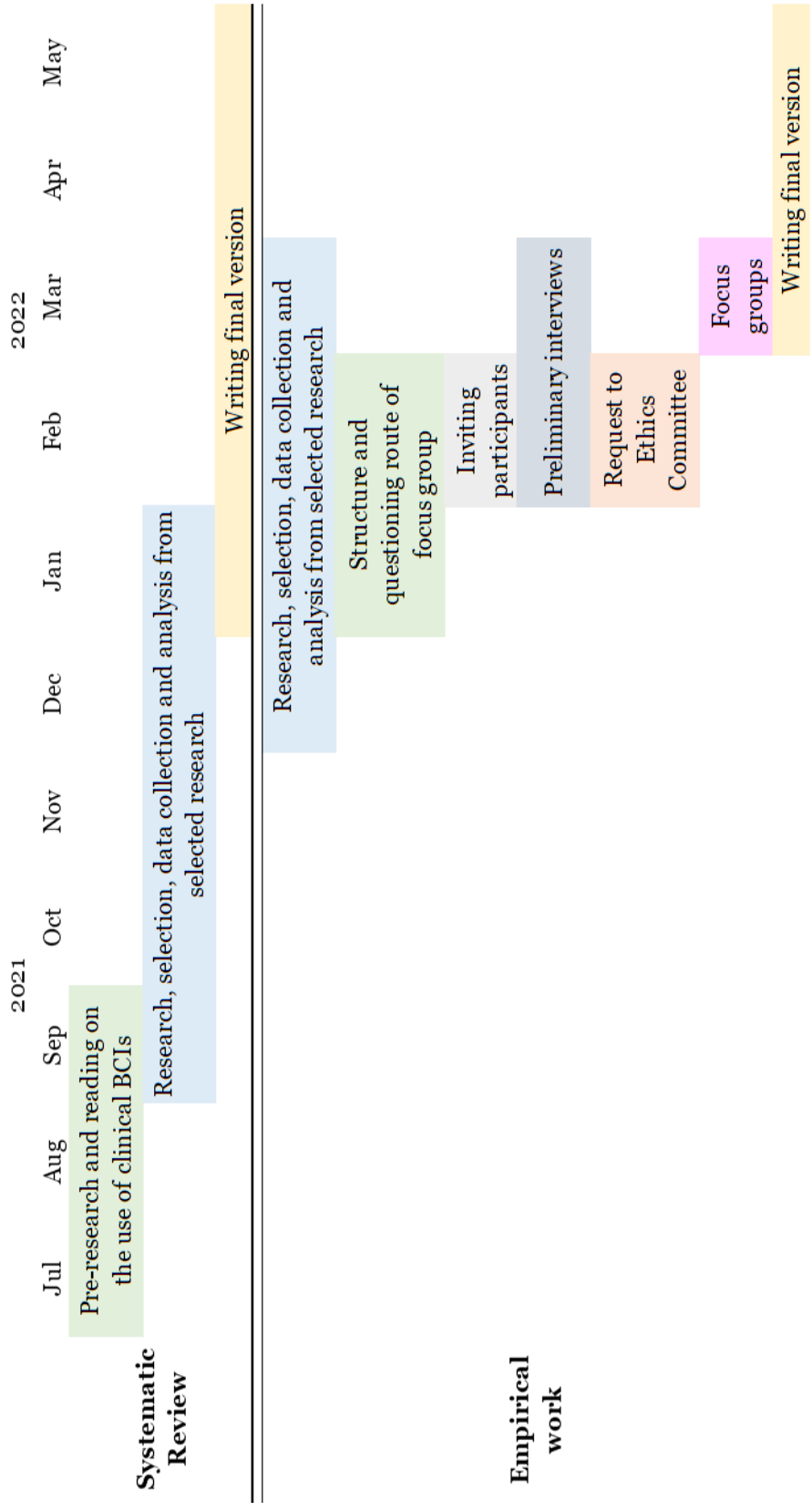
11. Appendixes

11.1. Appendix 1: Timeline



11.2. Appendix 2: Selected studies for systematic review

	Condition	Number of patients	Type of study	BCI	Year	Authors
1	Glaucoma	33	Trial	non-invasive	2017	Nakanishi M, Wang YT, Jung TP, et al. (69)
2	SCI (19 studies) Spinocerebellar degeneration (3 studies) ALS (2 studies) Brainstem stroke (1 study) Stroke (10 studies) Amputees (2 studies)	not specified	Review	both	2018	Bockbrader MA, Francisco G, Lee R, et al. (53)
3	Phantom limb pain	9	Clinical Trial	non-invasive	2018	Yanagisawa T, Fukuma R, Seymour B, et al. (65)
4	Stroke (upper limb)	233	Systematic review	non-invasive	2019	Carvalho R, Dias N, Cerqueira JJ. (56)
5	SCI	1	Phase I clinical trial	invasive	2019	Bockbrader M, Annetta N, Friedenberg D, et al. (59)
6	Stroke (upper limb)	7	Trial	non-invasive	2020	Chen S, Cao L, Shu X, et al. (63)
7	Stroke (upper limb)	14	Controlled trial	non-invasive	2020	Wu Q, Yue Z, Ge Y, Ma D, et al. (64)
8	SCI Stroke	not specified	Book chapter	both	2020	Pichiorri F, Mattia D. (58)
9	Stroke (upper limb)	10	Single-arm clinical study	non-invasive	2020	Bhagat NA, Yozbatiran N, et al. (57)
10	Stroke (upper limb-11 studies) (lower limb-2 study)	362	Meta-analysis	non-invasive	2020	Kruse A, Suica Z, Taeymans J, Schuster-Amft C. (54)
11	Stroke (upper limb-44 studies) (lower limb-6 studies) (cognitive impairments-12 studies)	592 61 247	Review	non-invasive	2020	Mane R, Chouhan T, Guan C. (33)
12	Stroke (upper limb-33 studies)	not specified	Meta-analysis	non-invasive	2020	Bai Z, Fong KNK, Zhang JJ, Chan J, Ting KH. (26)
13	LIS	not specified	Book chapter	both	2020	Vansteensel MJ, Jarosiewicz B. (55)
14	DOC	not specified	Book chapter	non-invasive	2020	Annen J, Laureys S, Gosseries O. (68)
15	ALS	82	Book chapter	non-invasive	2020	Vaughan TM. (61)
16	TBI	not specified	Book chapter	non-invasive	2020	Conde V, Siebner HR. (62)
17	SCI	not specified	Book chapter	both	2020	Rupp R. (52)
18	SCI	1	Case study	invasive	2021	Willett, F.R., Avansino, D.T., Hochberg, L.R. et al. (70)
19	Stroke (upper limb-18 studies) (lower limb-1 study)	not specified	Systematic review	non-invasive	2021	Camargo-Vargas D, Callejas-Cuervo M, Mazzoleni S. (3)
20	SCI	1	Case study	invasive	2021	Szymanski LJ, Kellis S, Liu CY, et al. (28)
21	Stroke (upper limb-30 studies)	208	Systematic review	non-invasive	2021	Baniqued PDE, Stanyer EC, Awais M, et al. (5)
22	DOC	14	Trial	non-invasive	2021	Eliseyev A, Gonzales IJ, Le A, et al. (67)
23	ALS LIS	not specified	Review	both	2021	Chaudhary U, Mrachacz-Kersting N, Birbaumer N. (21)
24	ADHD	not specified	Semi-systematic review	non-invasive	2021	Bravou V, Athanasios D. (66)
25	LIS - brainstem stroke	1	Trial	invasive	2021	Moses D, Metzger S, Liu J, et al. (60)

11.3. Appendix 3: AMSTAR 2 tool for systematic reviews

Potential clinical applications of BCIs in humans is a Critially Low quality review

1. Did the research questions and inclusion criteria for the review include the components of PICO?	Yes Yes Yes Yes Yes
2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	Partial YesYesYesYesYes
3. Did the review authors explain their selection of the study designs for inclusion in the review?	Yes Yes
4. Did the review authors use a comprehensive literature search strategy?	Partial Yes Yes Yes Yes Yes Yes
5. Did the review authors perform study selection in duplicate?	No
6. Did the review authors perform data extraction in duplicate?	No
7. Did the review authors provide a list of excluded studies and justify the exclusions?	No
8. Did the review authors describe the included studies in adequate detail?	No Yes Yes
9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review? **RCT**	No
NRSI	No

10. Did the review authors report on the sources of funding for the studies included in the review?	Yes Yes
11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results? **RCT**	0
NRSI	0
12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	0
13. Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?	Yes
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	Yes Yes
15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	0
16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	Yes Yes

Adapted from: Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. (2017)(48)

11.4. Appendix 4: COREQ checklist

No	Item	
Domain 1: Research team and reflexivity		
Personal Characteristics		
1.	Interviewer/facilitator	Diogo Neves
2.	Credentials	MD student
3.	Occupation	Student
4.	Gender	Male
5.	Experience and training	No previous experience in conducting focus groups
Relationship with participants		
6.	Relationship established	Some of the participants participate in a preliminary interview
7.	Participant knowledge of the interviewer	Aim of the research and credentials
8.	Interviewer characteristics	Positive bias towards BCIs, interest in technology and innovation in healthcare
Domain 2: study design		
Theoretical framework		
9.	Methodological orientation and Theory	Content analysis
Participant selection		
10.	Sampling	Purposive sampling
11.	Method of approach	Email
12.	Sample size	22 final participants (from 37 initial positive answers)
13.	Non-participation	9 invited guests dropped out due to schedule incompatibility. 6 lost to follow-up
Setting		
14.	Setting of data collection	Zoom Meeting
15.	Presence of non-participants	Not applicable (N/A)
16.	Description of sample	Participants from 9 countries, 3 continents. Background of Medicine, Engineering or mixed.
Data collection		
17.	Interview guide	Statements and prompts where only presented at the meeting
18.	Repeat interviews	N/A
19.	Audio/visual recording	Focus groups were recorded for following transcription and data extraction
20.	Field notes	N/A
21.	Duration	2 hours
22.	Data saturation	After the 3 focus groups carried out, there was evidence of some data saturation but not in all topics
23.	Transcripts returned	N/A
Domain 3: analysis and findingsz		
Data analysis		
24.	Number of data coders	N/A
25.	Description of the coding tree	N/A
26.	Derivation of themes	Themes and topics were identified in advance but also derived from the data
27.	Software	Zoom platform, version 5.9.7 (3931). Microsoft® Excel®, Microsoft 365 MSO (version 2202 Build 16. 0. 14931. 20128) 64-bit
28.	Participant checking	N/A
Reporting		
29.	Quotations presented	N/A
30.	Data and findings consistent	Yes
31.	Clarity of major themes	Yes
32.	Clarity of minor themes	Yes

Adapted from: Tong A, Sainsbury P, Craig J (2007)(49)

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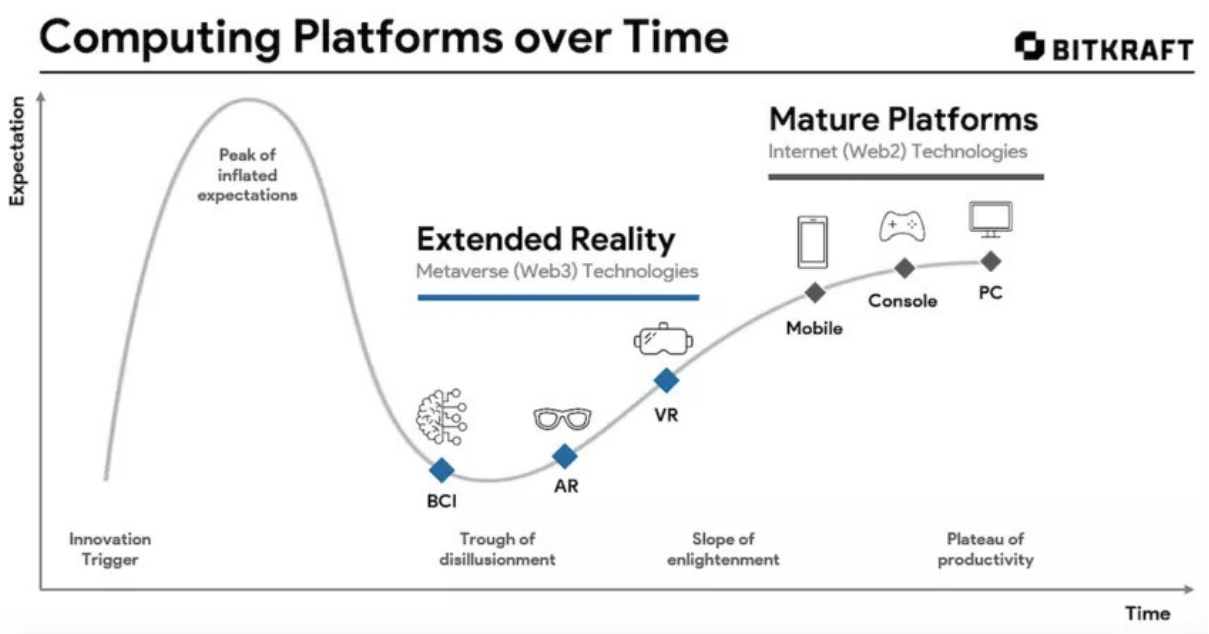
12. Annexes

12.1. Annex 1: Emergence of BCI as an extended reality technology (Hall SB, Baier-Lentz M. 2022)(23)



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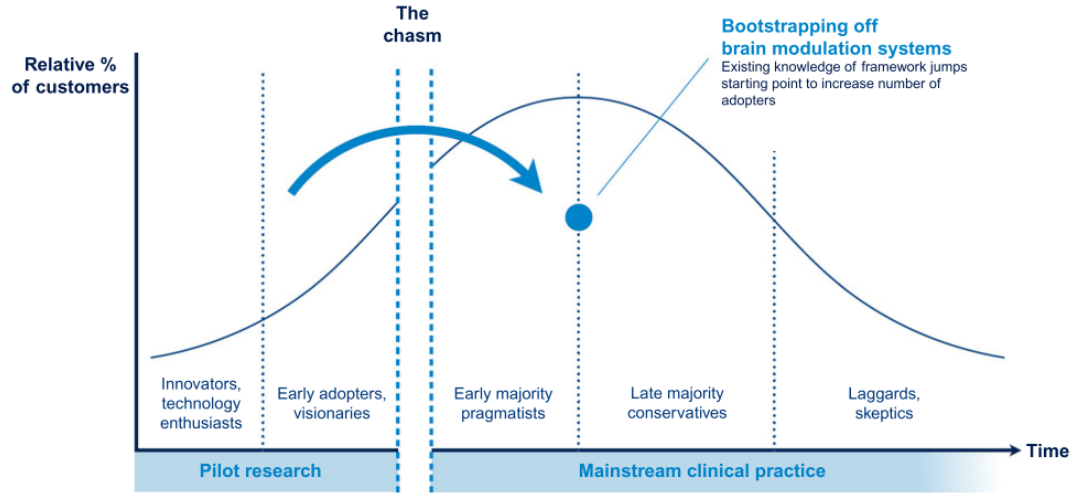
12.2. Annex 2: TALC and implications for translating BCIs into the clinic (Pulliam CL, Stanslaski SR, Denison TJ. 2020)(17)



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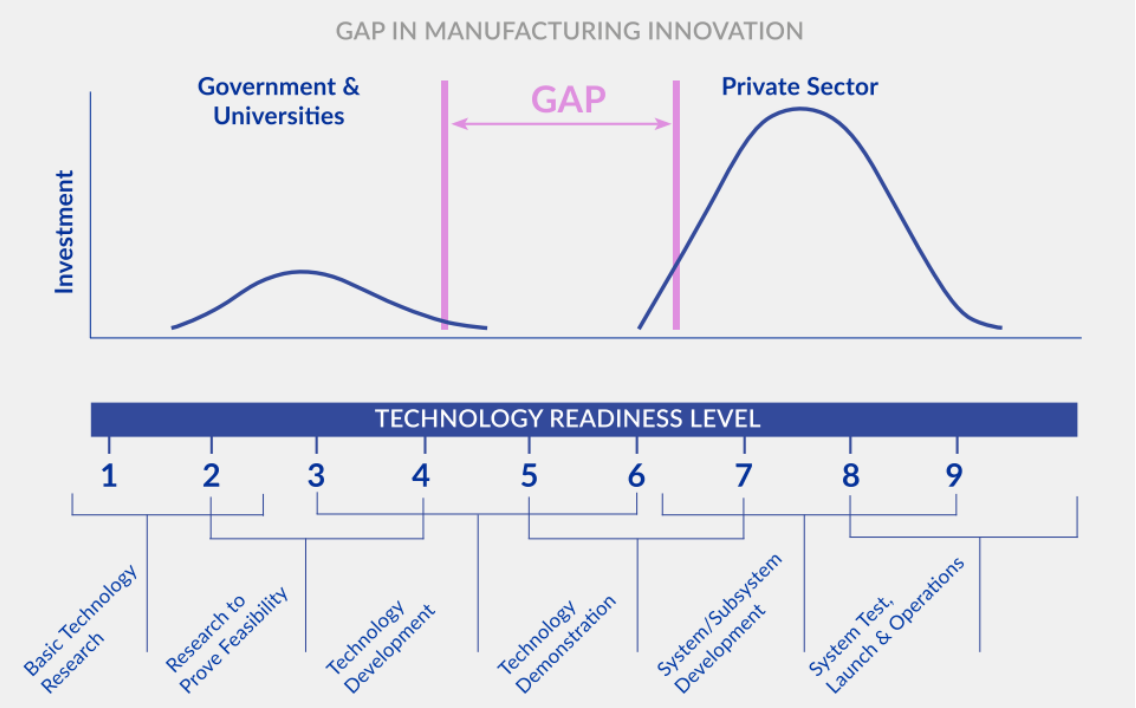
Additional Data

Portions	Figure 25.1 on page 342

12.3. Annex 3: Research-to-industry valley of death (Altimus C, Helmers-wegman E, Raver S. 2021)(12)

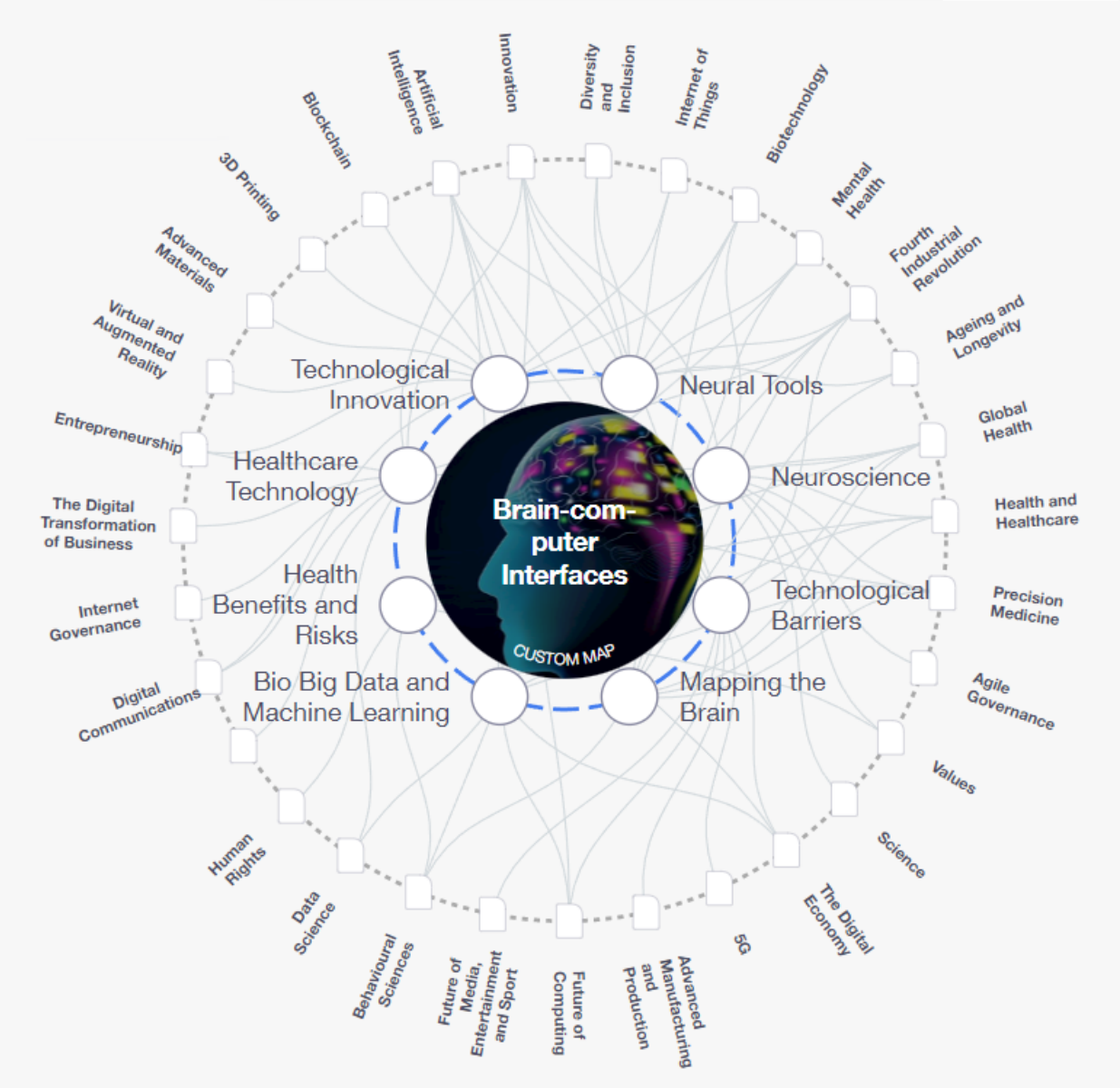


12.4. Annex 4: Transformation map for BCIs

A Transformation Map (or T-Map) is a visual representation of the strategic planning and execution process. T-Maps include important elements of successful strategic change: goals, actions, milestones, timelines, results, and impact. They are a dynamic way to explore and make sense of connections between industries, global issues and relevant topics.

With this is mind, The World Economic Forum (WEF) website was used to create a custom T-map with some of the topics related with BCIs and healthcare(78). Although this is a custom-made T-map, it is not personalized and therefore it was only possible to include previous issues generated by the WEF. Nonetheless, this show neurotechnology and Health Innovation are already key topics in our world and societies and the awareness is being raised, which is already a step towards a more innovation friendly health ecosystem.

WORLD ECONOMIC FORUM



12.5. Annex 5: UBI Ethics Committee approval

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Convento de Santo António
6201-001 Covilhã | Portugal

Parecer relativo ao processo n.º CE-UBI-Pj-2022-016-ID1227

Na sua reunião de 15 de março de 2022, a Comissão de Ética apreciou a documentação científica submetida referente ao pedido de parecer do projeto "**Brain-computer interfaces (BCIs): barriers and opportunities to potential clinical applications in humans**", do proponente **Diogo Filipe Vendeirinho Neves**, a que atribuiu o código n.º CE-UBI-Pj-2022-016.

Na sua análise não identificou matéria que ofenda os princípios éticos e morais, sendo de parecer que o estudo em causa pode ser aprovado.

Covilhã e UBI

A Presidente da Comissão de Ética

Assinado por : **ANA LEONOR SERRA MORAIS DOS SANTOS**
Num. de Identificação: BI112741975
Data: 2022.03.16 14:11:04+00'00'

CARTÃO DE CIDADÃO

(Professora Doutora Ana Leonor Serra Morais dos Santos)
(Professora Auxiliar)