Brain implants

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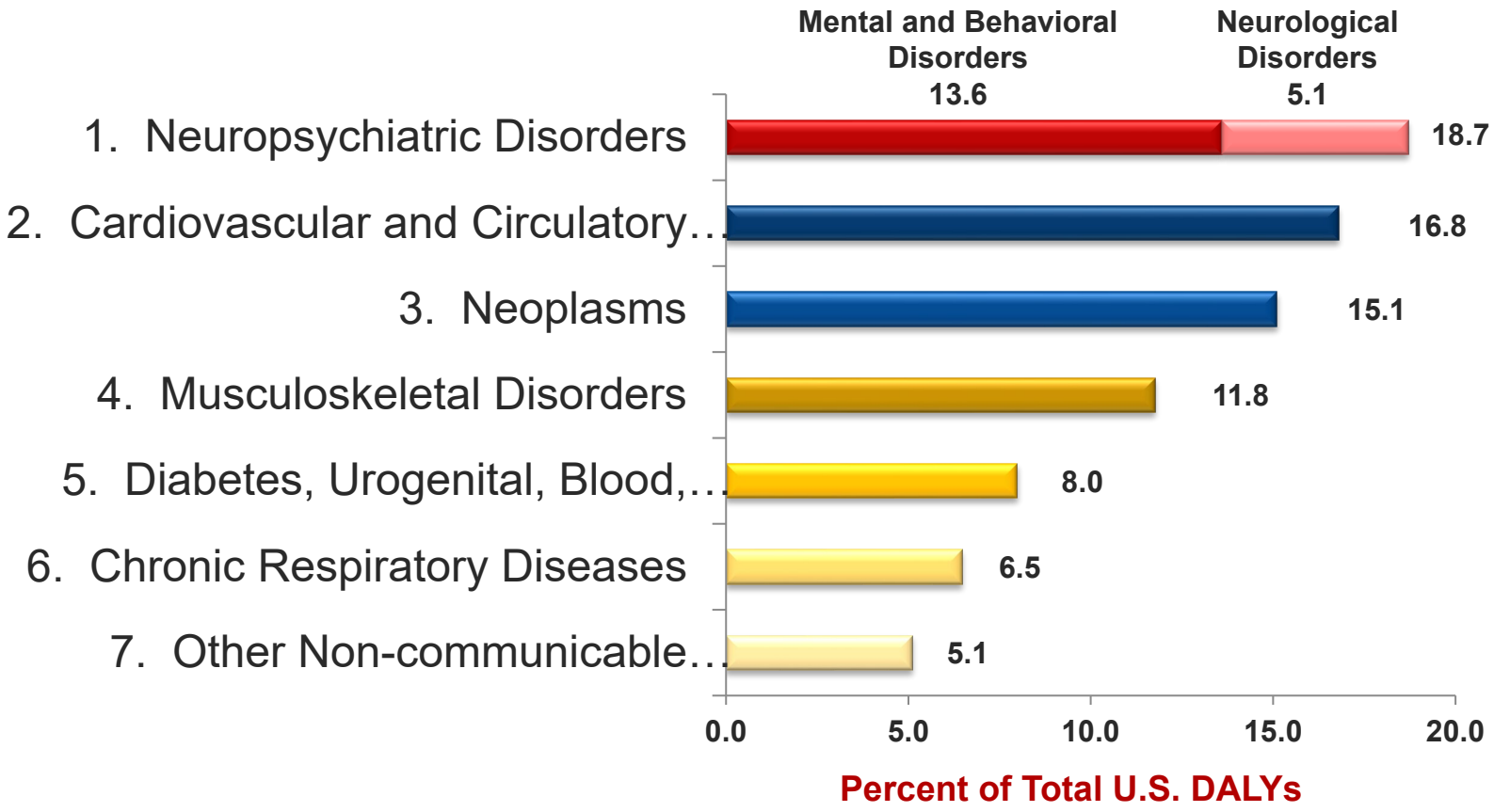
November 1, 2023

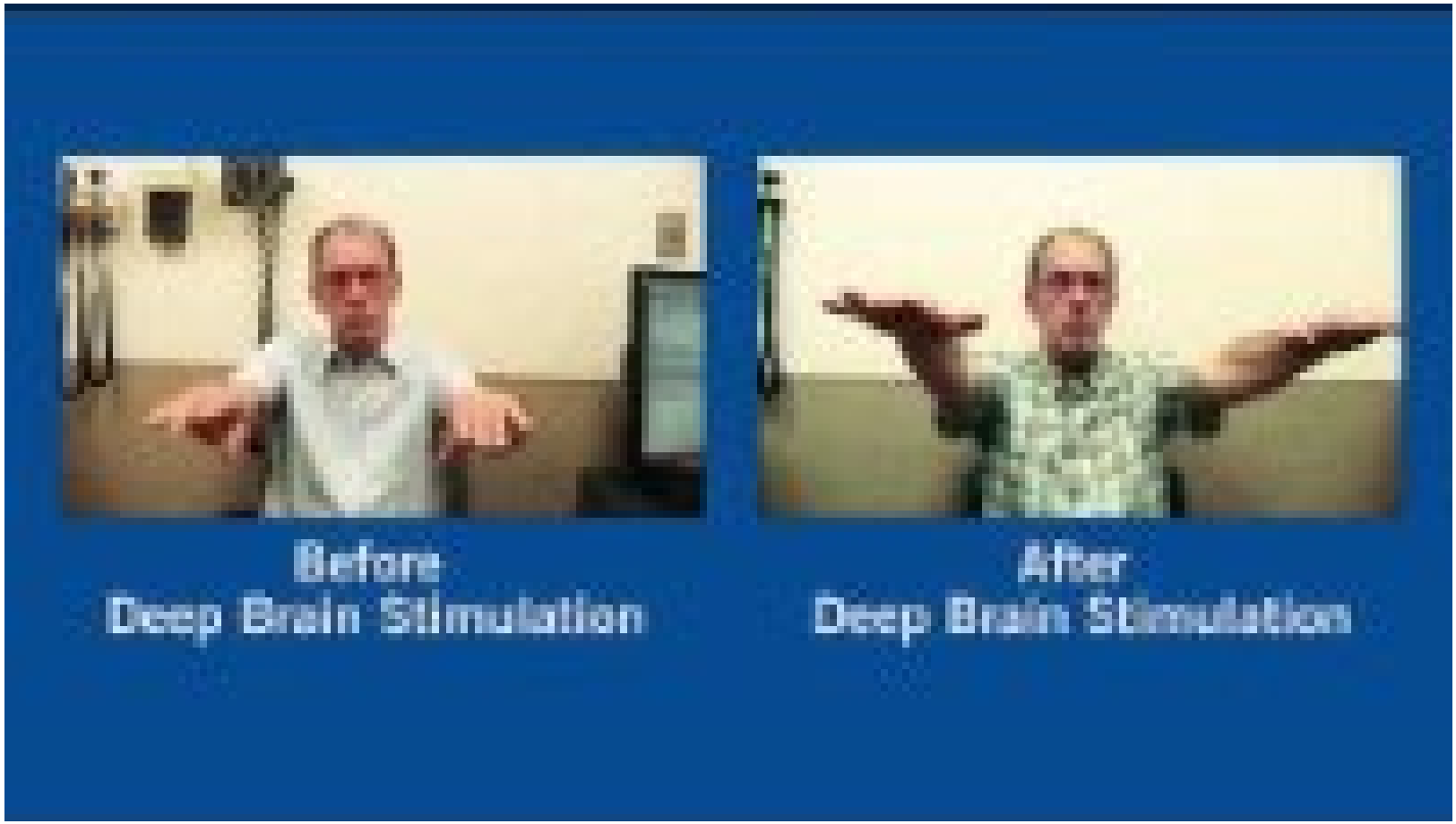
The views expressed are the my own and do not represent those of the NIH, the DHHS, or the US government.

Why we need the science to advance



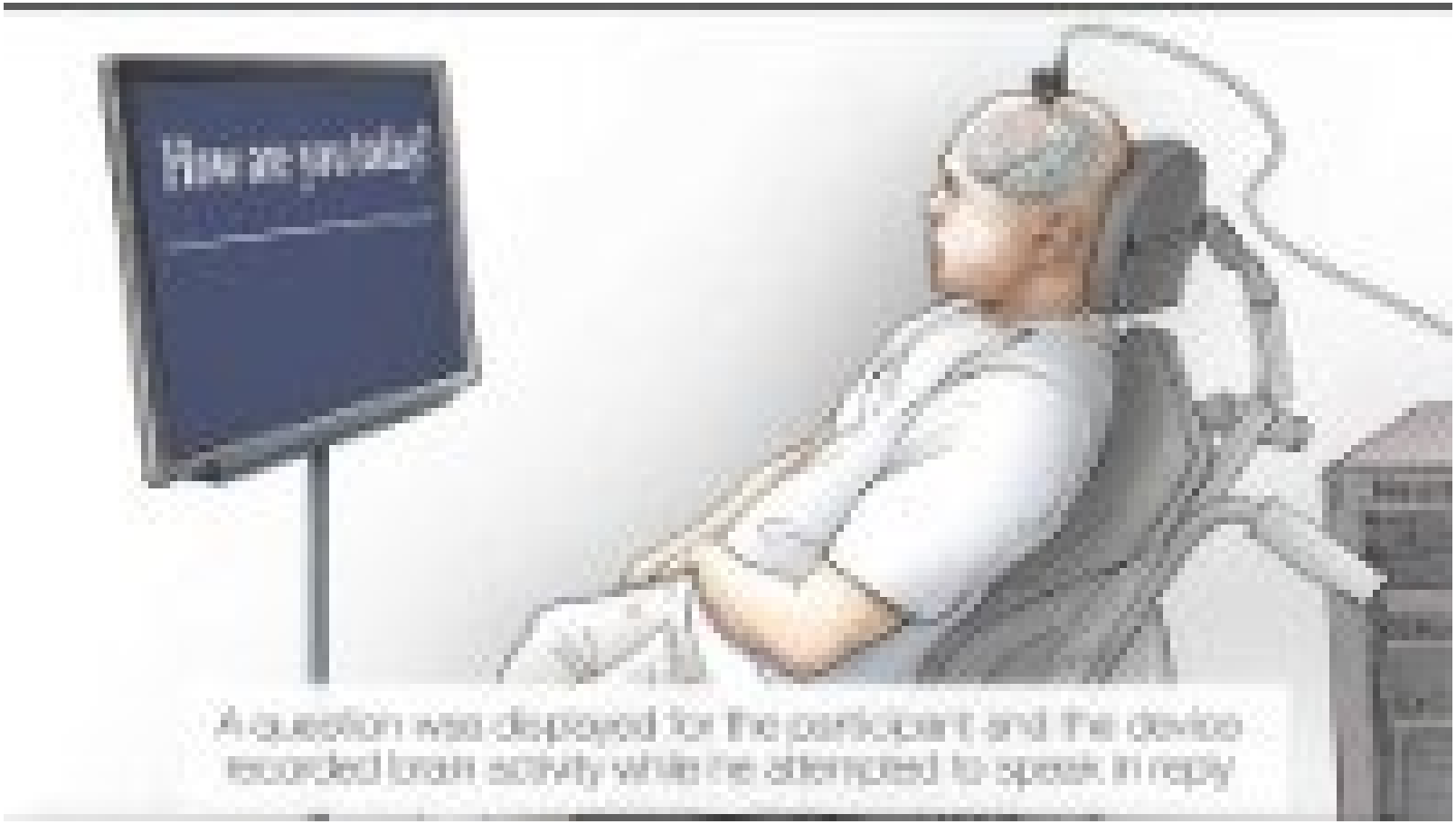
US Burden of Disease Collaborators, *JAMA*, 2013

Deep brain stimulation



Froedtert & the Medical College of Wisconsin

Speak neuroprosthesis



Existing guidance

- Research ethics guidance
  - Need specification and interpretation to address neural device research

The NIH Neuroethics Working Group identified ethics of human neural device research as a priority area

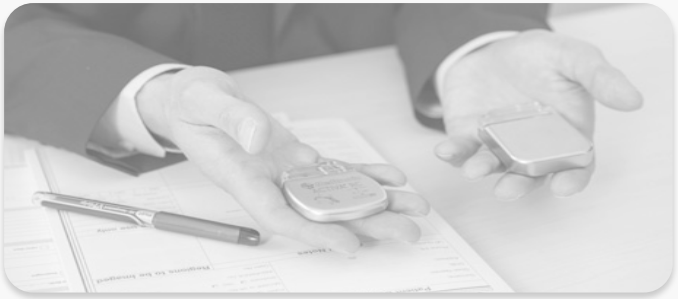
Ethical challenges in neural device research

Analysis of risk

Post-trial responsibilities

Ethical challenges in neural device research

Analysis of risk

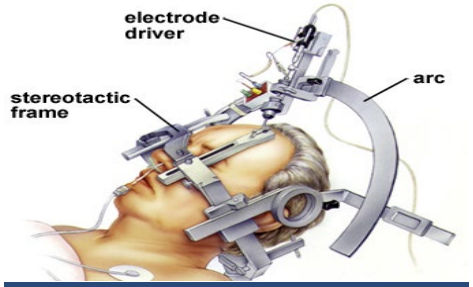


Post-trial responsibilities

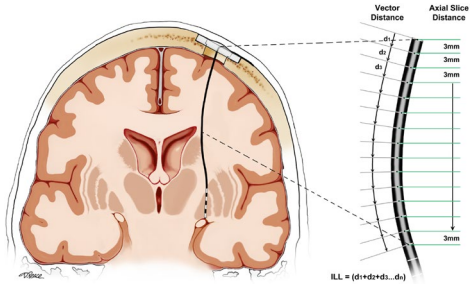
Identifying risk

- Research with invasive neural devices entails risk.
- Determining the type and extent of risk is fundamental to evaluating the ethics of neural device studies
  - Protect research participants from unnecessary harm
  - Inform risk/benefit evaluations (e.g., by IRBs)
  - Enable informed consent (Belmond, 1979; Emanuel et al, 2000)

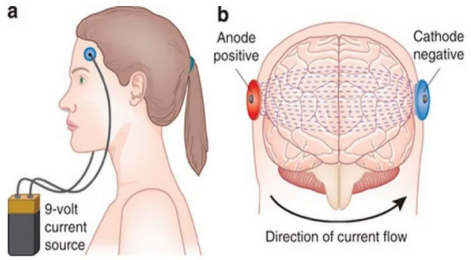
Sources of risk



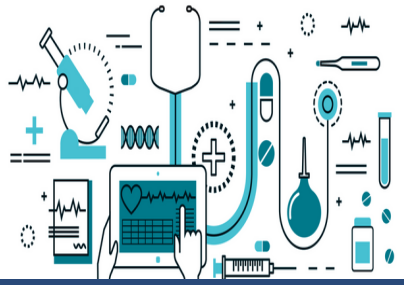
Surgery



Hardware



Stimulation



Research itself

Privacy and security

Financial burden

Evaluation of risks

For clinical research to be ethical:

- Potential risks to research participants should be minimized
- Potential benefits to participants and society are proportionate to, or outweigh, the risks (Emanuel et al, 2000)

Acceptable levels of risk are generally higher for studies that offer a possible therapeutic benefit for participants

Evaluation of risks

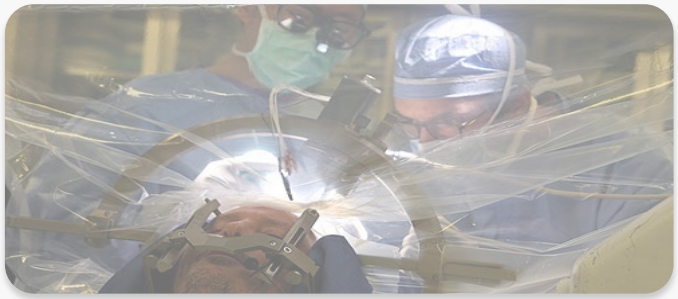
Research with a prospect of benefit

- Limits of acceptable risks are context-dependent
  - Anticipated benefits (e.g., severity of condition)
  - Vulnerable groups (e.g., consent capacity)

Research without a prospect of benefit

- Further research to clarify acceptable levels of risk
  - How much prolongation of surgery is acceptable for research?

Ethical challenges in neural device research



Analysis of risk

Post-trial responsibilities

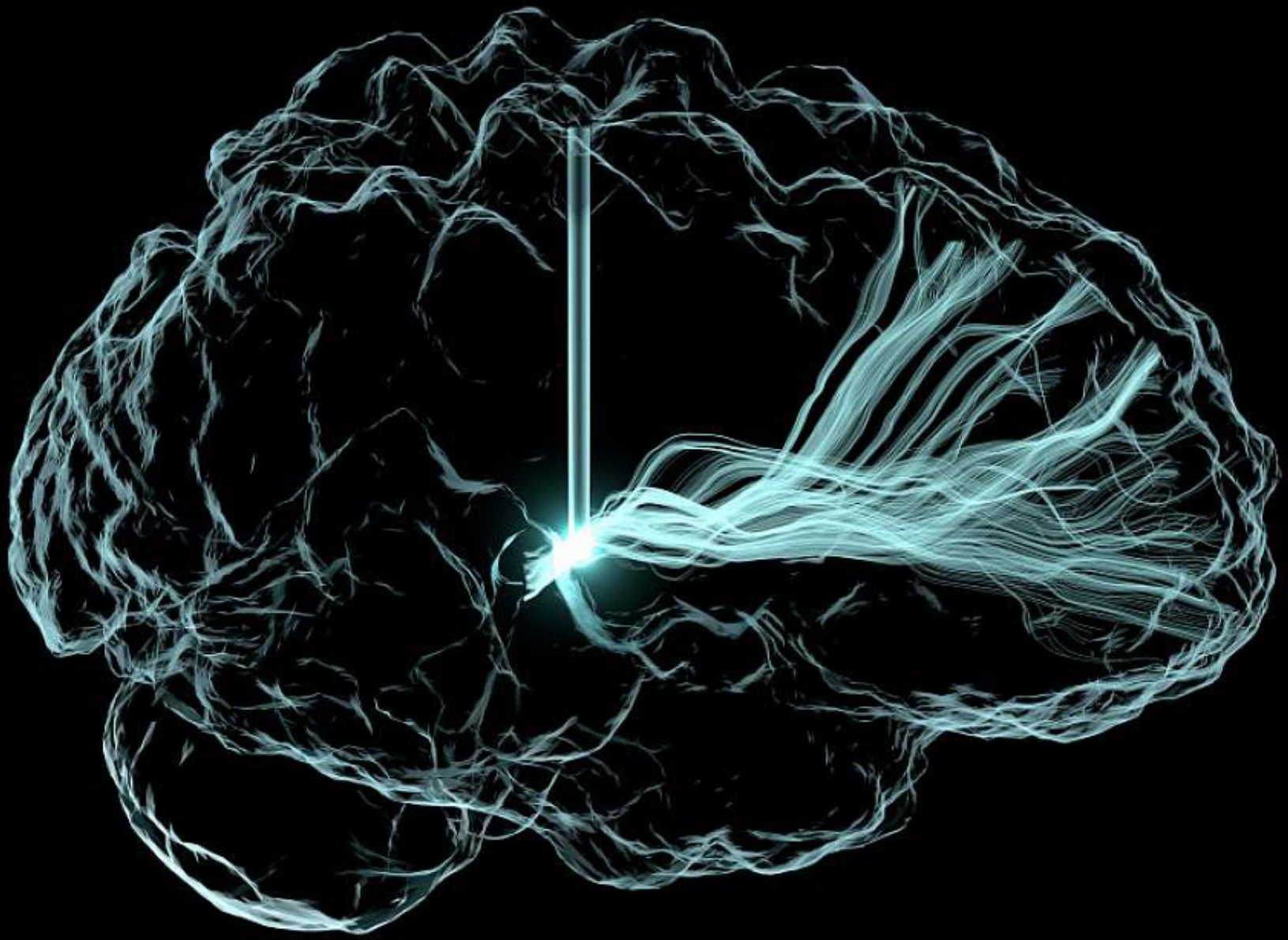


Image Courtesy of Andrew Janson, University of Utah Scientific Computing and Imaging Institute

Case 1

- Patient with severe treatment resistant epilepsy
- First in-human trial of BCI that predicts seizures
- Company folded, explantation recommended

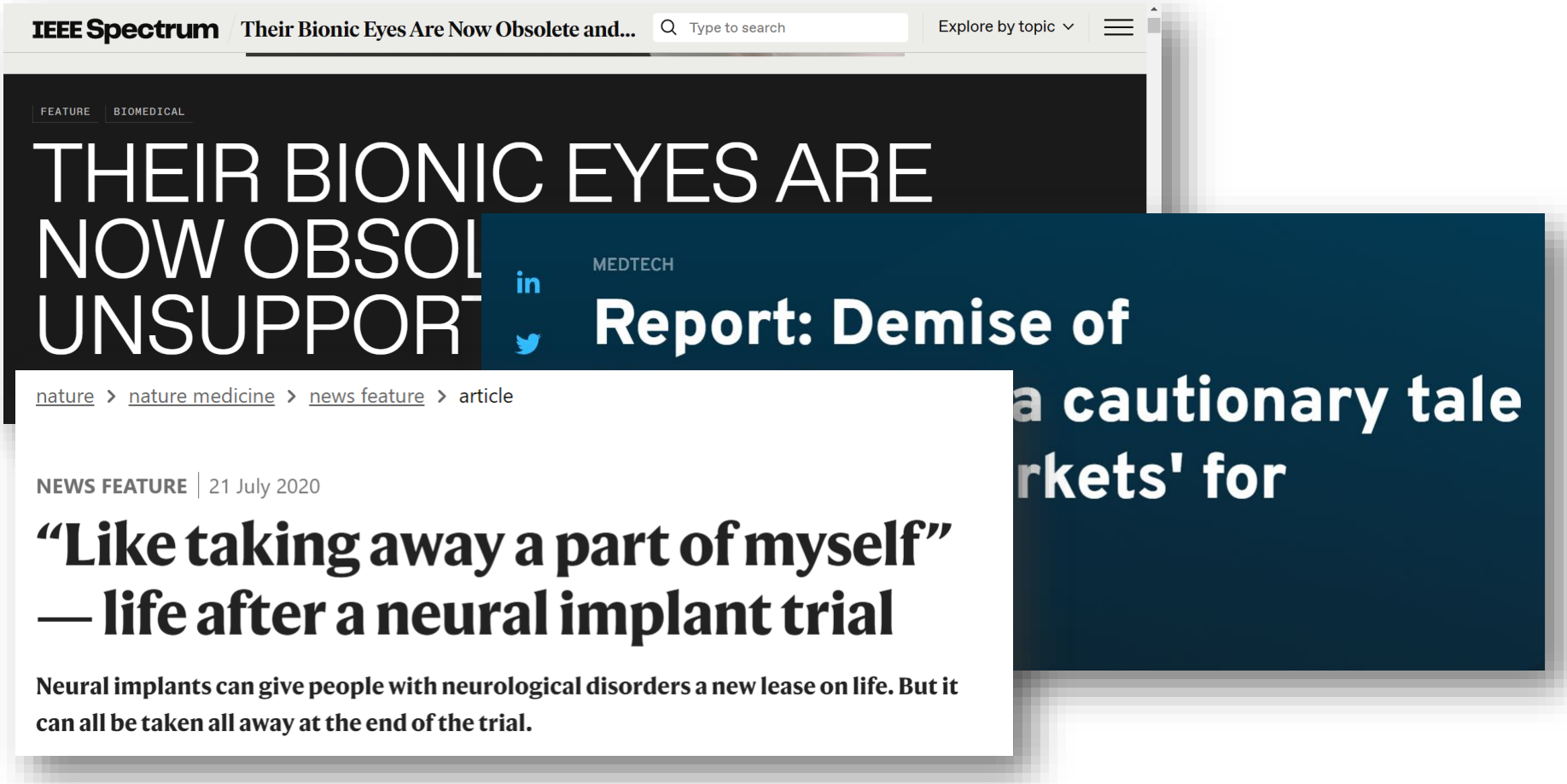
"I wish I could've kept it-I would've done anything to keep it. […] I wanted to stay with it […] I would've done anything-I would've paid money-I would've done anything if I could've. …

To this date, I have never again felt as safe and secure. Nor am I the happy, out-going, confident woman I was. … I always felt like there was something missing, I'd forgotten or left behind … a part of me!" (Gilbert et al., 2023)

Case 2

- Patient with treatment-resistant depression.
- Participates in DBS trial, and benefits.
- After the trial, she kept the device. The device is not yet FDA approved for this indication.

"For me, this device is not an experiment anymore. We know this works. This is the only thing that did work. If I need a battery replacement or a lead fixed or any one of those things… it's a way to keep me alive. …
So, I'm concerned about... I will never know, from one surgery to the next, if the next one will be covered by my insurance" (Hendriks et al., 2023)


IEEE Spectrum
Their Bionic Eyes Are Now Obsolete and...
Type to search
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FEATURE
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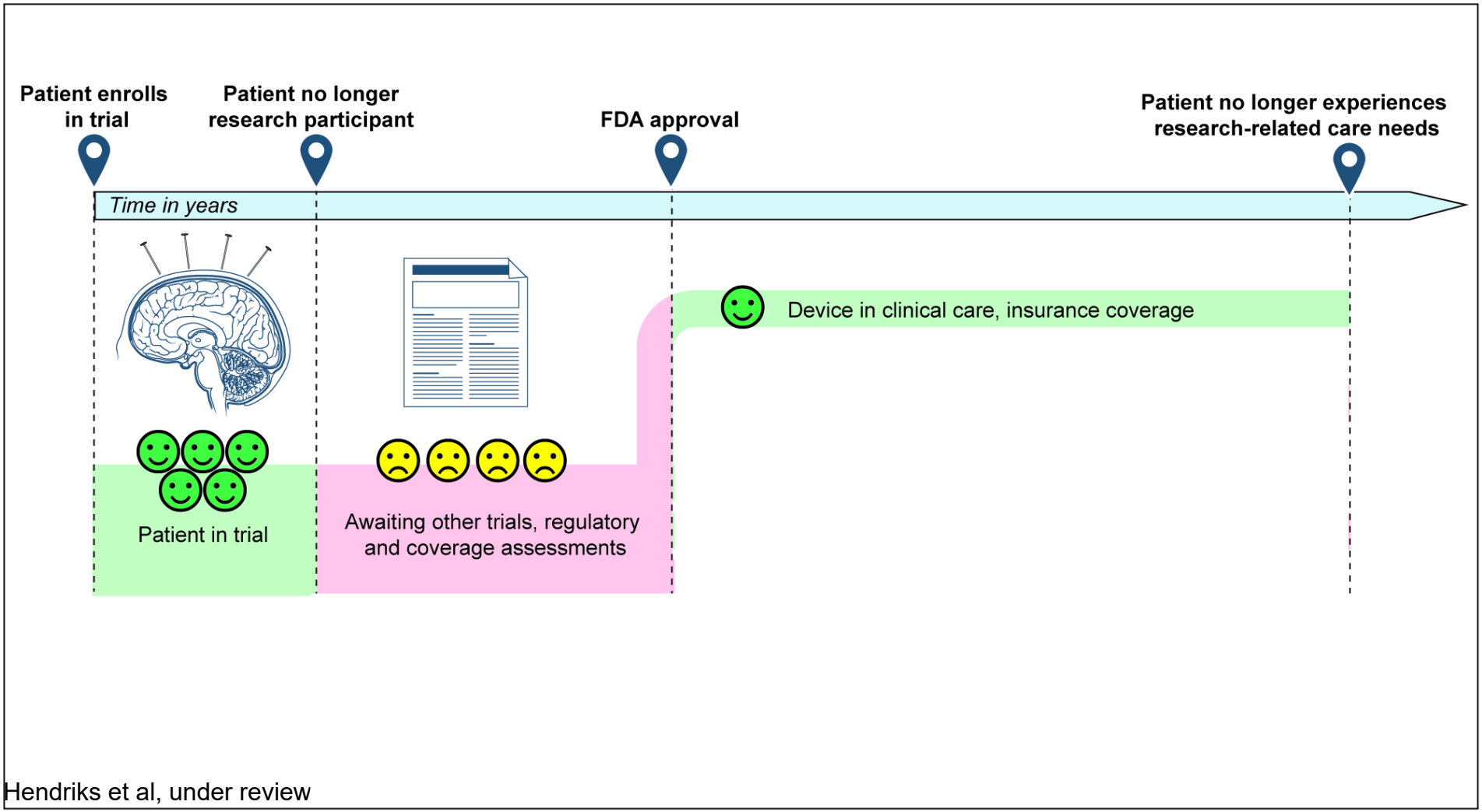
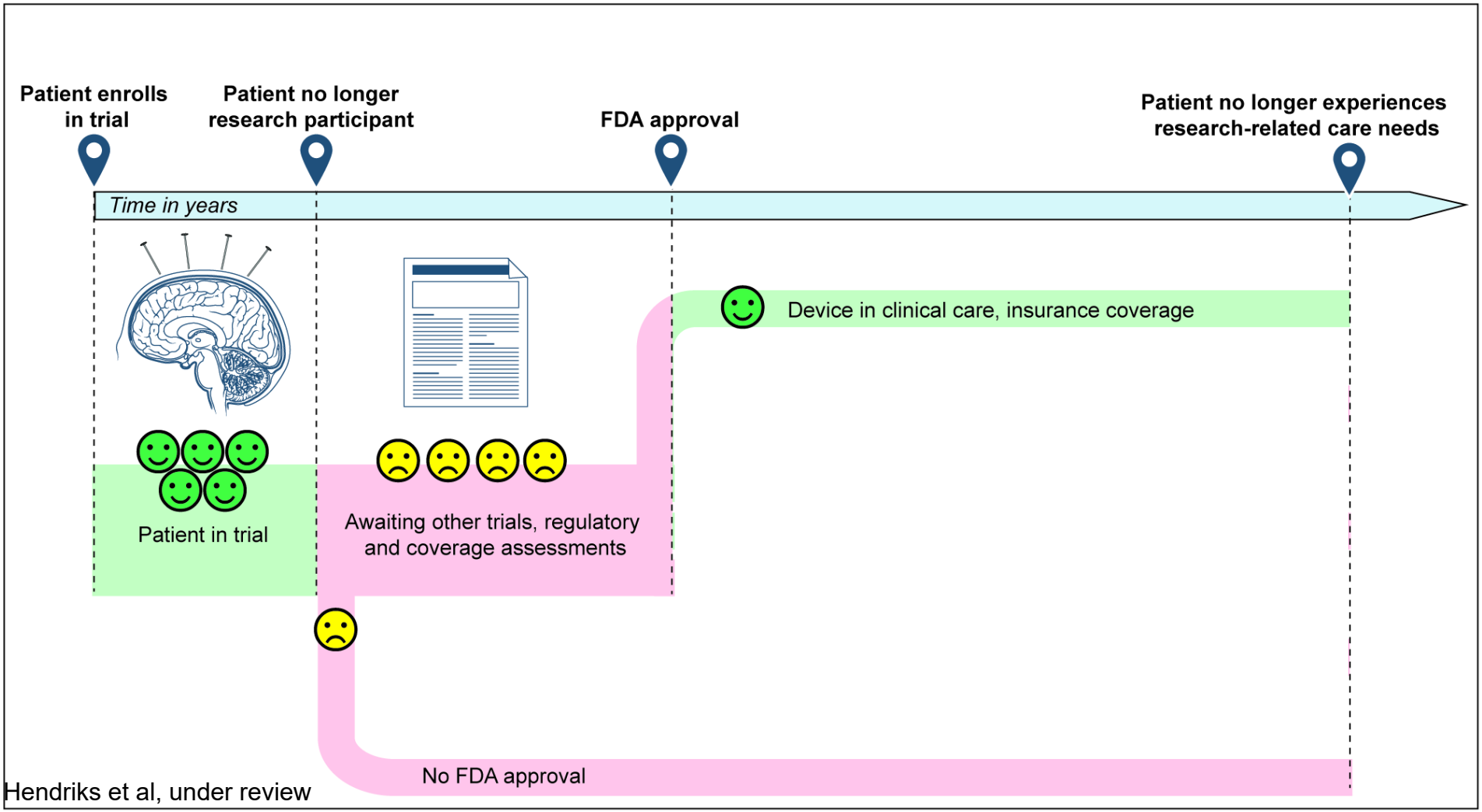
THEIR BIONIC EYES ARE
NOW OBSOL
UNSUPPORT
MEDTECH
Report: Demise of
a cautionary tale
rkets' for
nature > nature medicine > news feature > article
NEWS FEATURE | 21 July 2020
"Like taking away a part of myself"
— life after a neural implant trial
Neural implants can give people with neurological disorders a new lease on life. But it can all be taken all away at the end of the trial.

Different scenarios



Hendriks et al, under review

Different scenarios



Hendriks et al, under review

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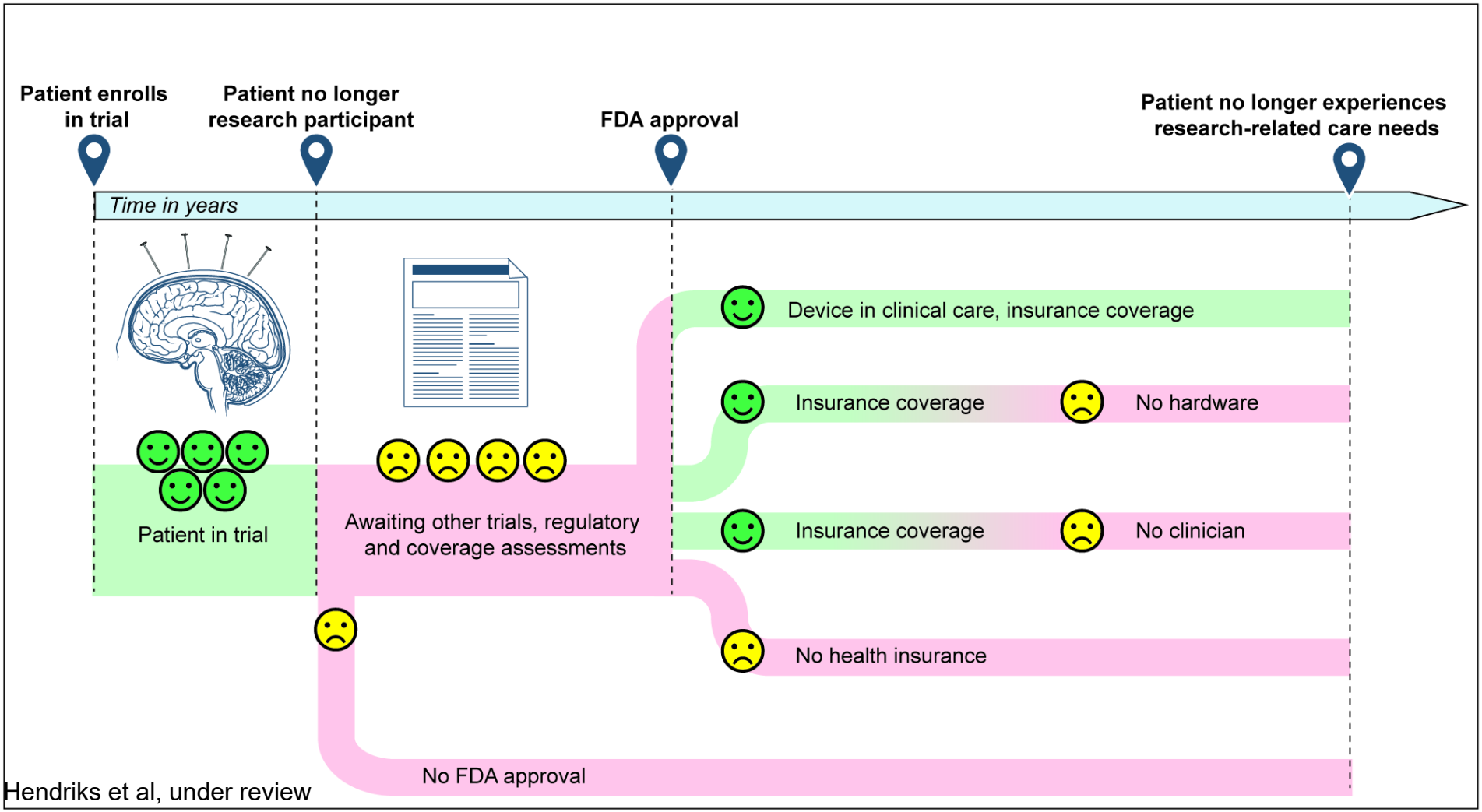


Hendriks et al, under review

What are met and unmet posttrial needs in neural implant trials?

Core posttrial needs (1)

- Anticipate and plan for posttrial needs
  - Some prospective participants consider a sufficient posttrial plan a condition for participation (Van Stuijvenberg et al., 2022)

- Disclosure about posttrial needs and plans
  - 6-month post-surgery, 33% (n =7) did not remember discussing continued access (Lazaro-Munoz et al., 2022)

(Hendriks et al., 2023)

Core posttrial needs (2)

- Continued access to an already-implanted device if
  - The patient is experiencing benefits
    - Almost all participants who benefited from the device (n=10), indicated that having the device explanted was not an option they considered (Sankary et al,. 2022)
    - 81% (n=17) participants thought they should get to keep the device (Lazaro-Munoz et al., 2022)
  - Risks of explantation outweigh risks of leaving the device in place

(Hendriks et al., 2023)

Posttrial needs for patients with a device

- Emergency care for complications related to the device
- Routine follow-up care and device support, maintenance, and repair:
  - Access to specialized clinicians
  - Removal and replacement of malfunctioning hardware
  - System and software updates
- Device explantation
  - because of a medical indication
  - elective

(Hendriks et al., 2023)

Concurrent posttrial needs

- Assistance coordinating care
- Accessibility of clinically relevant information for other clinicians outside of the specialized team
- Availability of research records for patients
- Mental health services related to trial participation

(Hendriks et al., 2023)

Current plans

- Each stakeholder has limits relating to their missions and resources
- Most current plans are a patchwork of conditional assurances
- Disagreements on what plans are appropriate and/or how responsibilities should be divided

(Hendriks et al., 2023)

What responsibilities, if any, do professional stakeholders have to facilitate or provide posttrial care?

Broader debates on posttrial care

No regulatory requirements.

Longstanding ethical debates on posttrial responsibilities, focused on pharmaceuticals

Why professional stakeholders may have posttrial responsibilities

Beneficence and non-maleficence

Reciprocity

Respect for persons

Relationship

Research participant: "It would be kind of cruel to give a guy this much life back and snatch it away just because of a few pennies, although it's more than a few pennies.'"

(Sarkar et al., 2022)

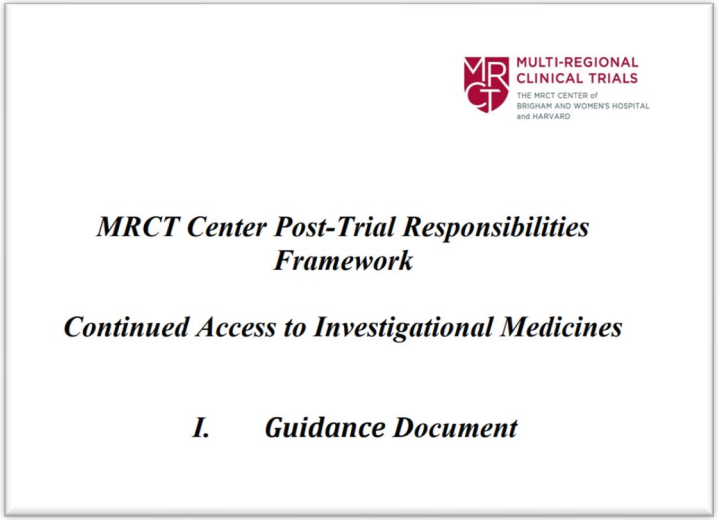
Research participant: "It felt like, hey look, let you implant things in my brain, I'm walking around with this, you have some responsibility to, um, you know, to look after me.'"

(Lazaro-Munoz, 2021)

Why stakeholders' responsibilities may have limits

Existing debates – consensus

- Some responsibilities exist
- Responsibilities have limits
- Responsibilities are shared among institutions and professionals involved in the trials


MULTI-REGIONAL CLINICAL TRIALS
THE MRCT CENTER of BRIGHAM AND WOMEN'S HOSPITAL and HARVARD

MRCT Center Post-Trial Responsibilities Framework

Continued Access to Investigational Medicines

I. Guidance Document

Challenges in operationalization and specification

'Investigational devices have unique challenges' (MRCT, 2017)

Weight of arguments for posttrial responsibilities and neural implants research

			
Beneficence and non-maleficence	Reciprocity	Respect for persons	Relationship
↑ Interests in receiving care	↑ Trials with high risks and burdens	↑ Lack alternatives ↑ Cannot benefit directly from the research	↑Trials with high risks and burdens ↑ Dependency ↑ Strong relationships

Implanted neural device trials – what's special?

- Continued risks after trial
- Higher-than-average research risks and burdens
- Dependency of implanted device trial participants
- Potential benefits
- Association with identity, personality, etc.

Posttrial responsibilities are higher in neural implant trials than in most drug trials

(Hendriks et al., 2023)

Neural implants vs other implants

- The factors that increase posttrial responsibilities for neural implants apply to some extent to other implants

- More gaps in posttrial care than other device trials
  - Relatively early stage - devices not FDA approved
  - Compatibility across manufacturers not established

(Hendriks et al., 2023)

Non-implanted devices

- Many of the factors that coalesce in *implanted* neural device trials to increase posttrial responsibilities are less common for non-implanted devices

(Hendriks et al., 2023)

Our recommendations

Neuron

NeuroView

Continuing trial responsibilities for implantable neural devices

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https://doi.org/10.1016/j.neuron.2023.07.008

Core posttrial responsibilities

- **Anticipate and plan for posttrial needs**
  - Funders, FDA, and/or IRBs recommend and/or assess long-term plans
- **Inform prospective participants**
  - Funders, FDA, and/or IRBs assess disclosure
  - Regulatory guidance?
- **Generally, let participants keep their implant when this is strongly in their clinical interest**

Posttrial responsibilities for patients with a device (1)

Facilitate access to emergency and routine care, minimize out-of-pocket costs

- Models for sharing cost:
  - Negotiate which stakeholder pays what piece, or
  - Stakeholders to pay into a specific **post-trial insurance, fund, or escrow**

- Consider policies or practices that allow coverage through health insurance based on individual-level benefit

Posttrial responsibilities for patients with a device (2)

Plan for reasonable access to clinicians, hardware replacements, and software update

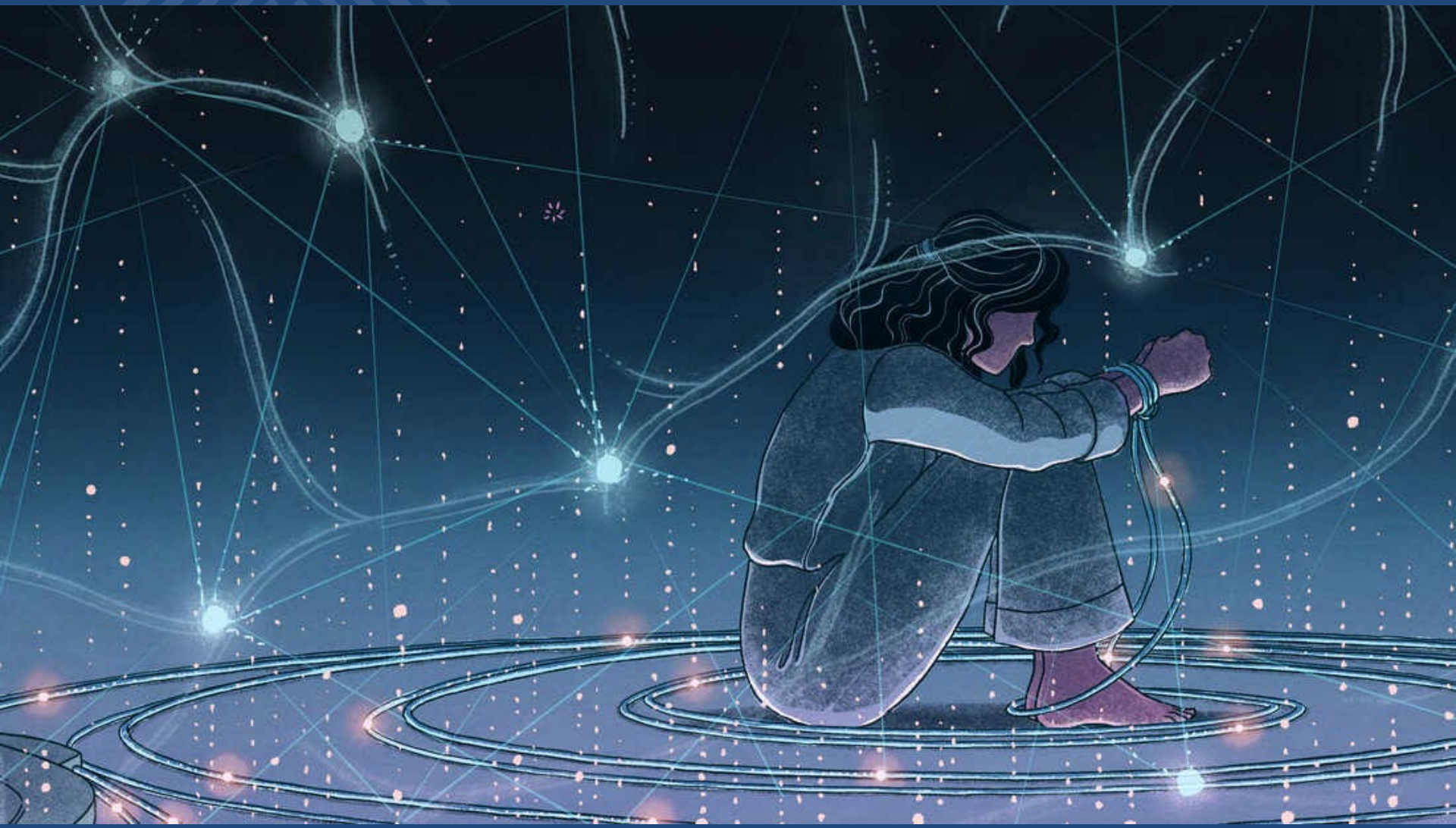
- Train a network of clinical specialists

- If possible, design devices to be compatible with commercially available hardware/software
- Agreements with other companies/nonprofits to cover responsibilities if manufacturer goes out of business
- Establish industry standards to ensure compatibility

Main concerns

- Main concern about supporting posttrial care is unduly affecting scientific progress
  - E.g., disincentivize companies and research institutions or move studies to other jurisdictions

- Feasibility should be considered when determining how responsibilities are operationalized and distributed
  - E.g., specifying limits in contributions and criteria for supporting posttrial care
- Incentives and other strategies to reduce potential deterrent effects



Christina Chung for NPR

Thank you

- Christine Grady, NIH CC
- Nina Hsu, NINDS
- John Ngai, The NIH BRAIN Initiative
- Andrea Beckel-Mitchener, The NIH BRAIN Initiative
- Members of the NIH BRAIN Initiative Neuroethics Working Group (NEWG)
- Workshop participants

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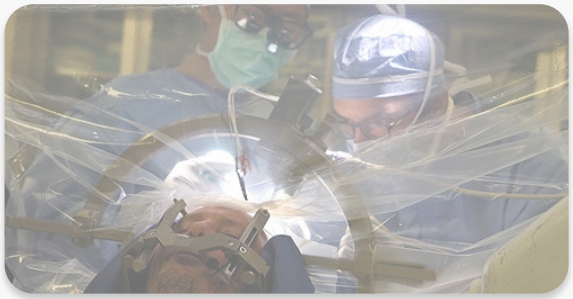
Ethical challenges in neural device research



Analysis of risk

Informed consent

Post-trial responsibilities

Informed consent

- Part of human subjects' protections
- Practical and theoretical challenges persist in obtaining informed consent

- Entails **disclosure of relevant information** to a **decisionally capable person** who makes a **voluntary decision** to enroll (Berg et al, 2001)

Disclosure

- Federal regulations: disclose of, e.g., reasonably foreseeable risks and benefits (45CFR46; 21CFR.50)

- What are reasonably foreseeable risks and benefits and how should they be disclosed?
  - Atypical risks (changes in behavior, personality etc.)

- Communicating effectively
  - Distinguishing between the research and standard care

Capacity

- Link between various brain disorders and impairments in
  - decision-making
  - decision-communicating

Voluntariness

- Does a lack of therapeutic options influence voluntariness?
- Do dual roles (clinician-researcher) make some participants feel unable to decline participation?