Posttrial responsibilities to participants in neural device research

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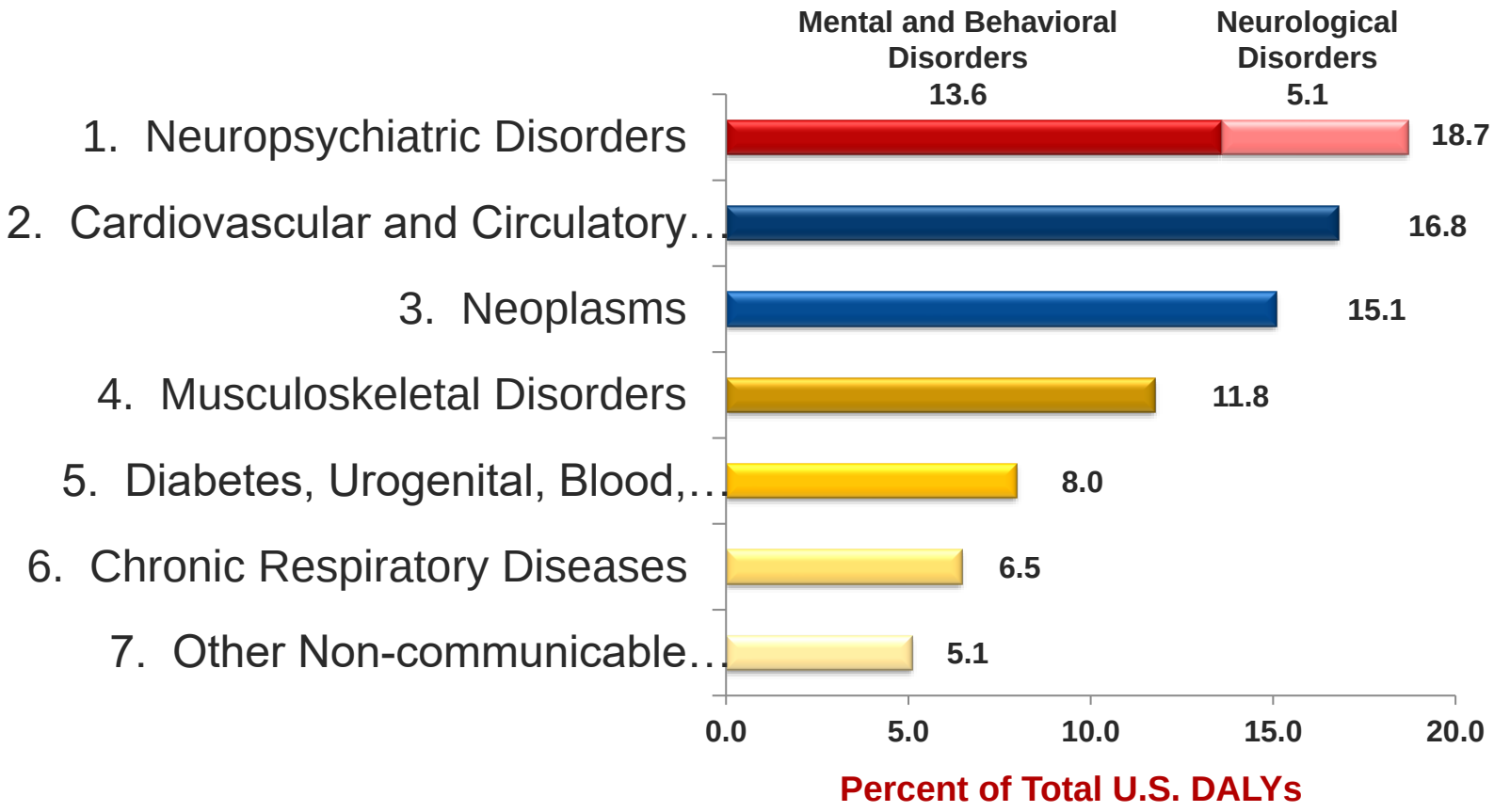
The views expressed are the my own and do not represent those of the NIH, the DHHS, or the US government.

Learning objectives

- Appreciate the debate about posttrial responsibilities more broadly and how devices pose novel challenges
- Describe posttrial needs for participants of neural device trials
- Understand the ethical arguments for and against posttrial responsibilities in device trials
- Consider the weight of these arguments for different types of needs and different types of trials
- Appreciate currently available options and potential future strategies for reducing unmet posttrial needs

Why we need the science to advance



US Burden of Disease Collaborators, *JAMA*, 2013

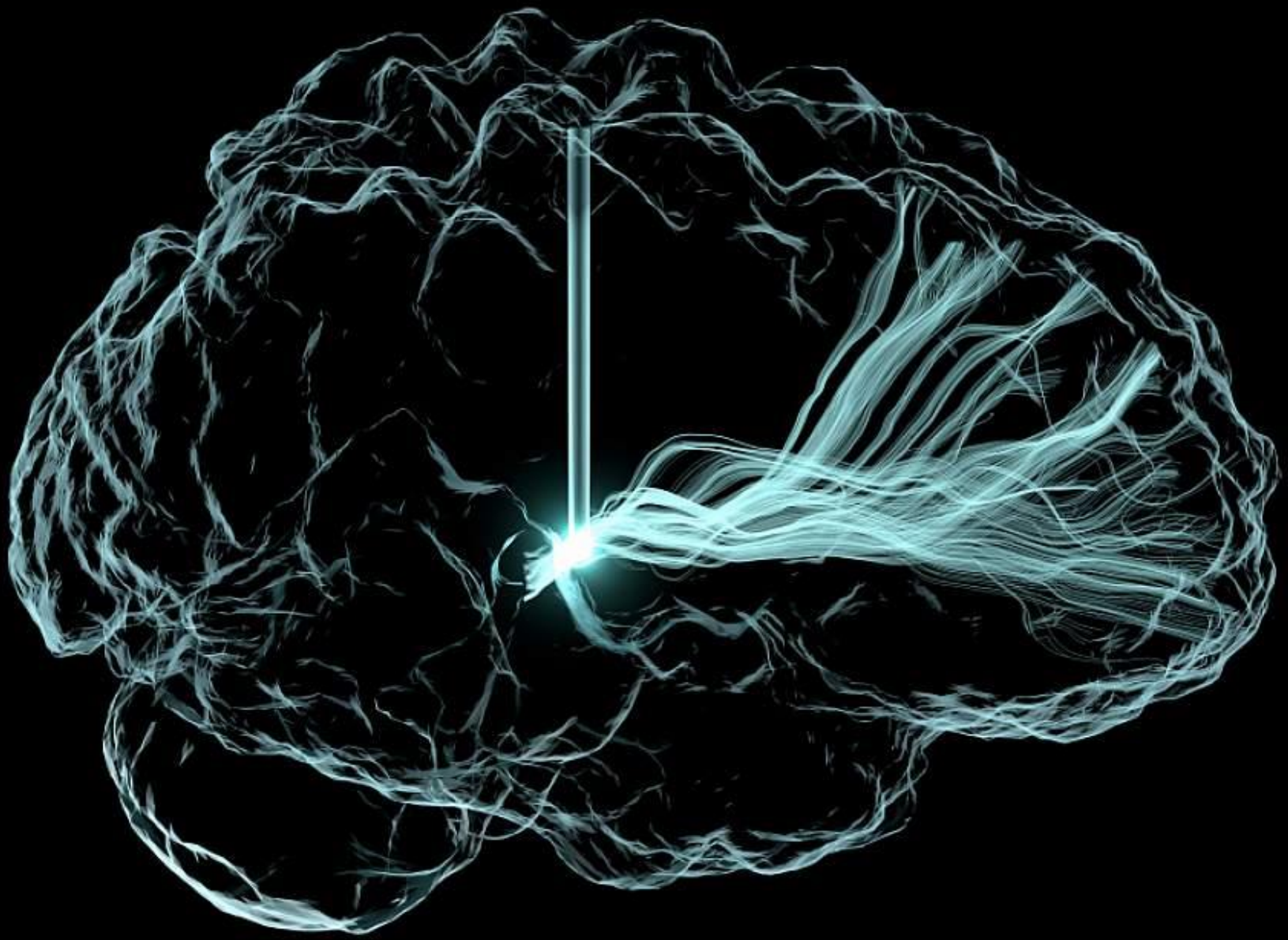


Image Courtesy of Andrew Janson, University of Utah Scientific Computing and Imaging Institute

Case 1

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

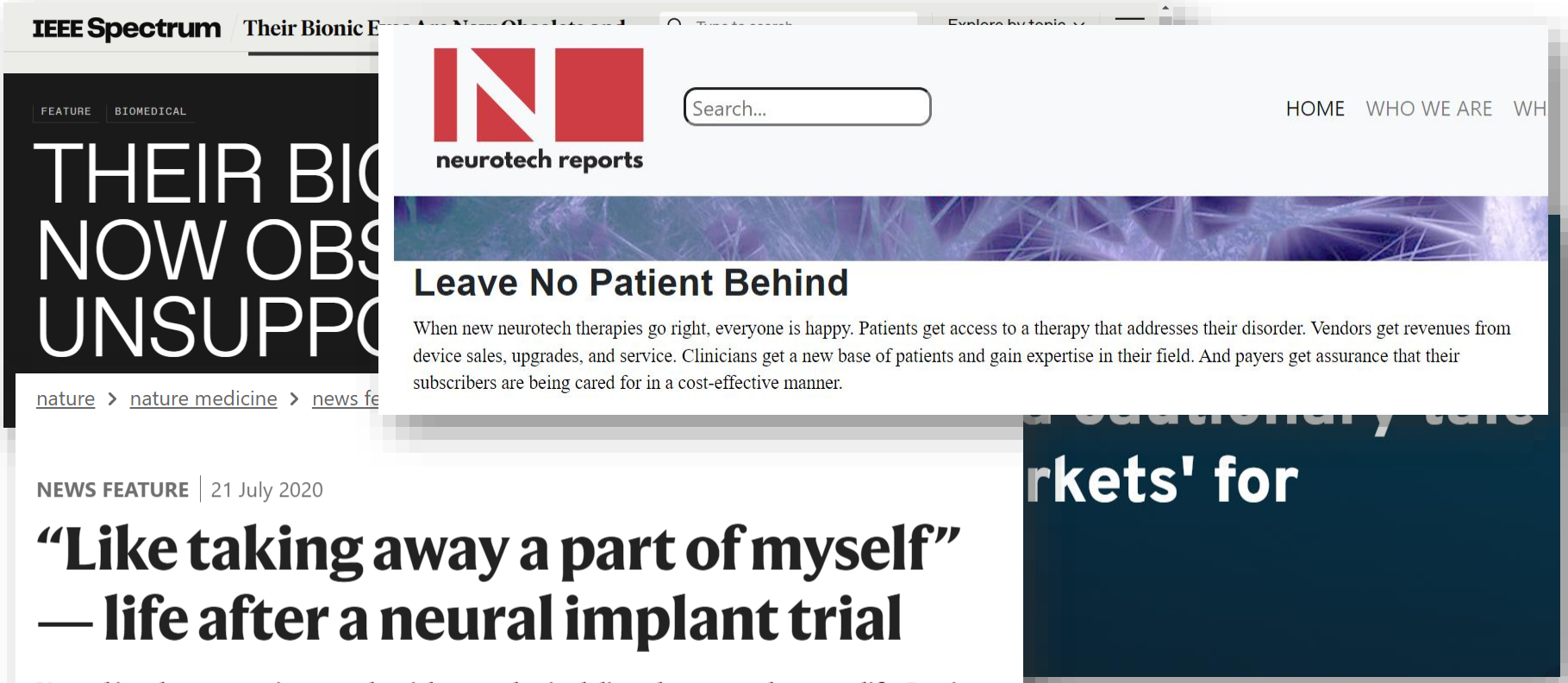
"I wish I could've kept it-I would've done anything to keep it. […] I wanted to stay with it […] I would've done anything-I would've paid money-I would've done anything if I could've. …

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)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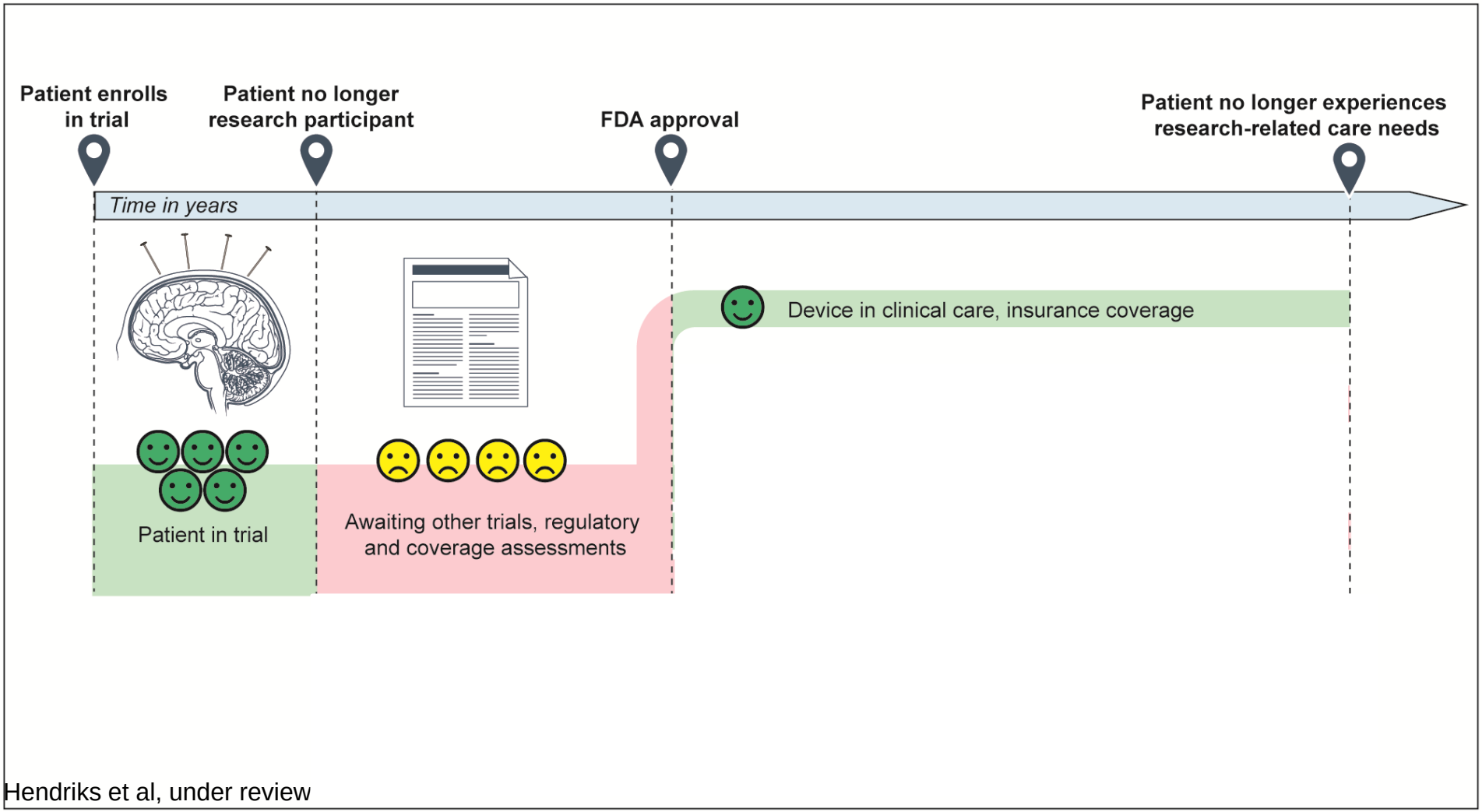
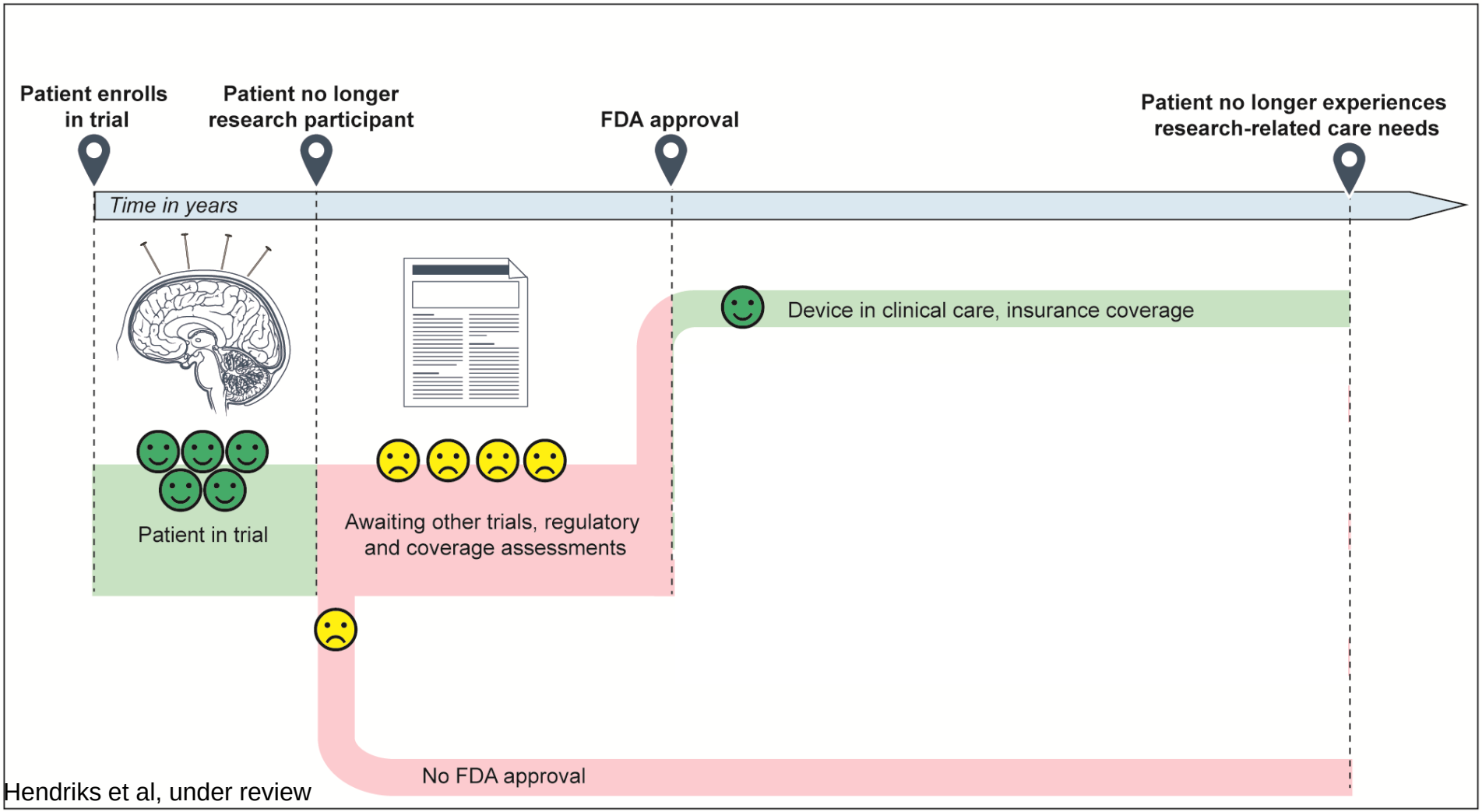
Leave No Patient Behind
When new neurotech therapies go right, everyone is happy. Patients get access to a therapy that addresses their disorder. Vendors get revenues from device sales, upgrades, and service. Clinicians get a new base of patients and gain expertise in their field. And payers get assurance that their subscribers are being cared for in a cost-effective manner.
nature
nature medicine
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



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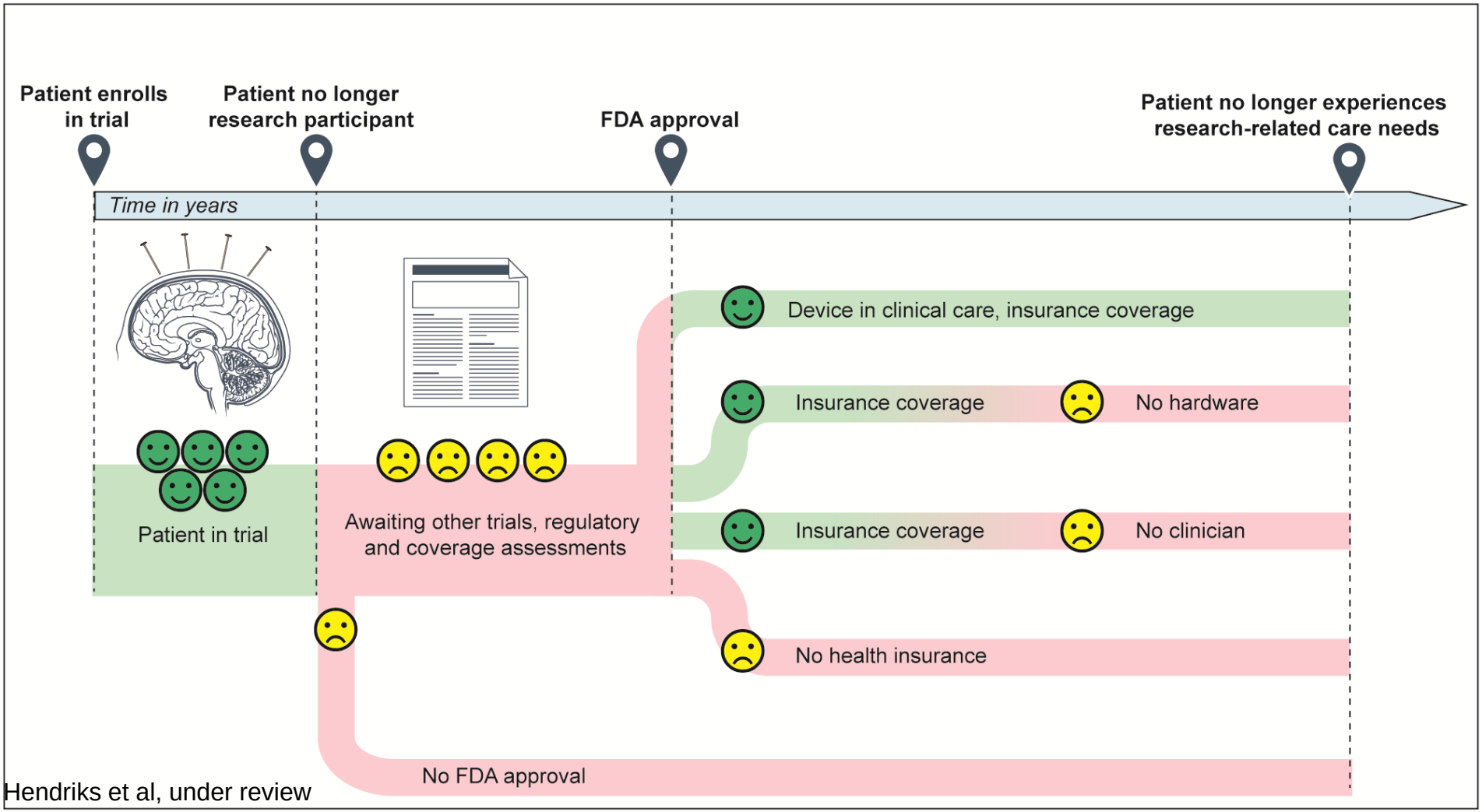
Different scenarios

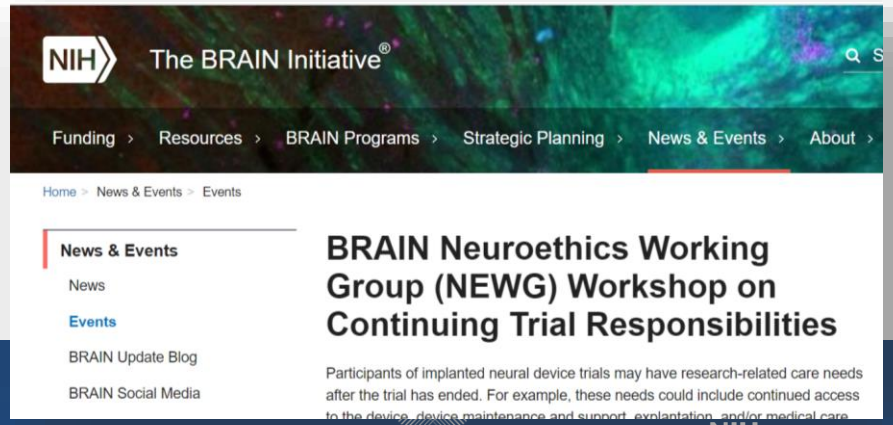


Hendriks et al, under review

Methods/sources

- Literature review
- Information-gathering dialogues held by NIH with stakeholder groups (Dec 2021-April 2022)
- BRAIN Neuroethics Working Group workshop (May 2022)
- BRAIN Neuroethics Working Group closed discussion (Aug 2022)
- Normative analysis

(Hendriks et al., 2023)



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)
  - Participants who kept the implant expected access to follow-up care and device hardware replacements (Sankary et al,. 2021)

(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

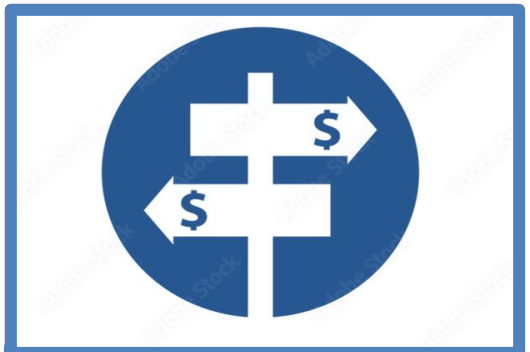
Respect for persons

Relationship

Research participant: "It would be kind of cruel to give a guy this thing in his brain and then walk away just because of a few pennies, although it's more than a few pennies." (Lazaro-Munoz et al., 2022)

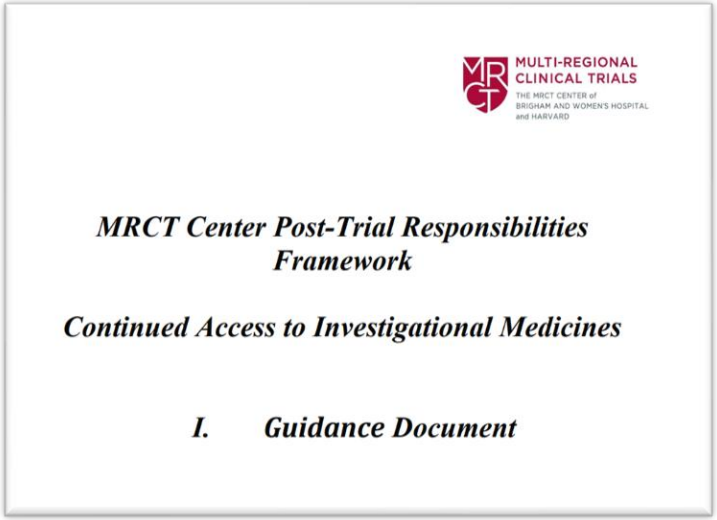
Research participant: 'It felt like, hey look, I let you implant things in my brain, I'm taking a risk with you here, you have some responsibility to me, you know, to look after me.' (Sankary et al., 2021)

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 implanted device 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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Special consideration

- Responsibilities that are grounded in non-maleficence

- Needs that are uniquely dependent on one stakeholder
  - Clinician-investigators to receive highly-specialized care
  - Device manufacturers to produce replacement hardware and software updates

(Hendriks et al., 2023)

Proposed responsibilities: core posttrial needs

- Researchers, device manufacturers, funders, and others should anticipate and plan for posttrial needs, and inform prospective participants

- Patients should get to keep their implant in most cases when:
  - The patient is experiencing ongoing and significant benefits
  - Risks of explantation outweigh risks of leaving the device in place

Strategies to consider: core posttrial needs (1)

Planning for posttrial care

- Map out the patient journey
- Funders, FDA, and/or IRBs recommend and/or assess long-term plans
- Consider incentives for supporting posttrial care
- If possible, design devices for safe explantation and compatibility with diagnostic and therapeutic tools

Strategies to consider: core posttrial needs (2)

Consent

- Funders, FDA, and IRBs assess disclosures of posttrial needs and plans
- Regulatory guidance

Keeping implant

- If not covered by insurance: involved parties explore device donation and/or providing financial support
- Minimize risks of inactive devices that are too risky to explant

Proposed responsibilities: posttrial needs for patients with a device

Facilitate access to care, minimize out-of-pocket costs:

- Emergency care for complications related to the device
- Follow-up care and device support, maintenance, and repair:
  - Access to specialized clinicians
  - Removal and replacement of malfunctioning hardware
  - System and software updates

  Ensure reasonable number
- Device explantation
  - Because of a medical indication
  - Elective

Strategies to consider: posttrial needs for patients with a device

- 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

Strategies to consider: posttrial needs for patients with a device (continued)

- Reduce risk of lacking access to hardware, software
  - 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

- Reduce risk of lacking access to specialized clinicians
  - Provide training, establish a network of specialists
  - Simplify device control systems

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

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- Workshop participants

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