



# Is the Treatment Worse than the Disease?: Key Stakeholders' Views about the Use of Psychiatric Electroceutical Interventions for Treatment-Resistant Depression

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**Abstract** Psychiatric electroceutical interventions (PEIs) use electrical or magnetic stimulation to treat psychiatric conditions. For depression therapy, PEIs include both approved treatment modalities, such as electroconvulsive therapy (ECT) and repetitive transcranial magnetic stimulation (rTMS), and experimental neurotechnologies, such as deep brain stimulation (DBS) and adaptive brain implants (ABIs). We present results from a survey-based experiment in which members of four relevant stakeholder groups (psychiatrists, patients with depression, caregivers of adults with depression, and the general public) assessed whether treatment with one of four PEIs (ECT, rTMS, DBS, or ABIs) was better or worse than living with treatment-resistant depression (TRD) and then provided a narrative explanation for their assessment. Overall, the prevalence of many narrative

themes differed substantially by stakeholder group—with psychiatrists typically offering different reasons for their assessment than non-clinicians—but much less so by PEI modality. A large majority of all participants viewed their assigned PEI as better than living with TRD, with their reasons being a mix of positive views about the treatment and negative views about TRD. The minority of all participants who viewed their assigned PEI as worse than living with TRD tended to express negative affect toward it as well as emphasize its riskiness, negative side effects, and, to a lesser extent, its invasiveness. The richness of these narrative explanations enabled us to put in context and add depth to key patterns seen in recent survey-based research on PEIs.

**Keywords** Depression · Neuromodulation · Perceptions · Stakeholder · Vignette experiment · Survey

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## Introduction

Major depressive disorder is a serious mental health problem that has been increasing in prevalence in the United States in recent years [1]. While the majority of patients can be treated with psychotherapy or antidepressant medication, a substantial percentage does not respond to antidepressants [2]. As such, mental health professionals increasingly see potential in psychiatric electroceutical interventions (PEIs)—therapies that use electrical or magnetic stimulation to the brain—for dealing with treatment-resistant depression (TRD). Electroconvulsive therapy (ECT) has high rates of response among patients with TRD [3], but does not work for all such patients [4]. More recently, repetitive transcranial magnetic stimulation (rTMS) has been approved as a safe and effective treatment for TRD [5, 6]. Beyond these approved therapies, deep brain stimulation (DBS) has been tested in several clinical trials that target different locations in the brain; however, these trials have been inconclusive [7–9].

The use and future development of PEIs raise several ethical issues that must be addressed. These include practical concerns about the interventions' safety and effectiveness [8, 10–15], how these interventions might affect aspects of users' sense of self [16–18]—including a large literature on personality [19, 20], identity [21], agency and autonomy [22, 23], and authenticity [24]—as well as considerations related to barriers to access [25–28]. There are also broader questions about social attitudes related to depression and to the use of PEIs [29–34].

Given that some of these therapies are new and not well-known by patients and the public, and that ECT often elicits especially visceral negative reactions from non-clinicians [30, 35], it is important to understand how these treatments are viewed by different stakeholder groups. Our recent research aims to better understand different stakeholder groups' views on four PEIs: ECT, rTMS, DBS, and a variation on DBS—closed-loop DBS or adaptive brain implants (ABIs). Here, we present a portion of our survey data that asks participants for their comparative assessment of treatment with one of these four PEIs with life with TRD. We also include participants' narrative explanation of their response to this survey question. We discuss these results in light of

recent findings in the literature on the use of electroceuticals in mental health.

## Experimental Methods

### Study Design

Building on work in experimental neuroethics [36, 37], we used the contrastive vignette technique [38] to explore different stakeholders' attitudes toward PEIs for addressing TRD. We collected responses via a standardized survey, with an embedded video vignette experiment, that we administered online via Qualtrics to four large US samples of the general public, caregivers, depressed patients, and psychiatrists. We collected this survey data between April and June 2020.

We randomly assigned participants to view one of eight video vignettes composed of orthogonally rotated primary [modality: ECT, rTMS, DBS, ABI] and secondary [depression severity: moderate, severe] independent variables, resulting in a  $4 \times 2$  between-subjects design. We intended to compare attitudes on the use of different PEIs across the two levels of depression. For our purposes here, we focus solely on assigned PEI modality. However, we do report selected results for depression severity in Tables OR3 and OR4 in the Online Resources file.

We crafted the vignettes to ensure that they were minimally contrastive and depicted a plausible representation of a conversation between a psychiatrist and patient, so that the results would be responsive to the hypotheses under consideration. We used second-person vignettes in order to reduce actor-observer asymmetries that can bias responses [39]. We analyzed the vignettes using the Flesch-Kincaid Reading Ease and Grade Level readability tests, confirming that their text would be comprehensible to 15- to 21-year-olds. We employed cognitive interviews during pre-testing to ensure that participants understood the vignettes' narrative [40].

### Participants

We contracted with Qualtrics to assist in the sampling of non-clinician participants. Qualtrics recruited

1,022 adults from the general public to match the US Current Population Survey's estimates of age, sex, race, and income characteristics of the US adult population in spring 2020. Qualtrics applied a screening question in addition to the population estimate matching to select 1,026 adult caregiver stakeholders who were currently serving as the primary caregiver for someone with depression. For our last non-clinician group, Qualtrics drew a quota sample of 1,050 adults with depression from a separate internet panel of adults who previously reported a depression diagnosis. Our patient sample matched age, sex, and race estimates of the US adult population living with depression.

Our research team managed the recruitment and sampling of our psychiatrist stakeholder group. Briefly, using a sampling frame of all 49,431 psychiatrists listed in the American Board of Psychiatry and Neurology directory in mid-October 2019, we generated a contacted sample of 16,190 psychiatrists that was stratified by state residency. Ultimately, 505 board-certified psychiatrists submitted completed surveys. For more details, please see [citation removed for blinding]. Table OR1 in the Online Resources file presents selected socio-demographic characteristics for each of the four stakeholder groups.

### Key Survey Questions

After participants viewed their assigned video vignette and answered a few questions to assess their comprehension of it, they then answered several sets of questions measuring their attitudes and beliefs about the PEI in their video vignette (i.e., their "assigned PEI").<sup>1</sup> Following this, they answered the following two questions which are our focus here. "[PEI]" is a placeholder for text that was inserted according to their experimental condition: ECT, rTMS, DBS, ABIs.

Think about the symptoms of treatment-resistant depression and what you now know about [PEI]. Which phrase below BEST captures your current thinking on these?

Overall, I think [PEI] seems \_\_\_\_\_ than living with treatment-resistant depression.

- ☐ much worse than
- ☐ slightly worse than
- ☐ the same as
- ☐ slightly better than
- ☐ much better than

In the comment box below, please FULLY EXPLAIN your answer to the PREVIOUS QUESTION.

The more details that you provide, the better we will understand your reasoning—which is crucial for our research project.

### Analytical Techniques

We conducted our analyses with IBM SPSS 29.0. We performed a series of one-way analysis of variance (ANOVA) tests with Tukey's honestly significant difference (HSD) tests to examine the differences in mean responses to the first, closed-ended question across stakeholder groups and assigned PEI modality. Table OR3-OR9 in the Online Resources file have the results for the post-hoc Tukey Honestly Significant Difference (HSD) tests. Following the steps described in Cabrera et al. 2015 [41], we used Contrastive Quantitized Content Analysis (CQCA) to analyze variation in responses to the second, open-ended question across stakeholder groups and assigned PEI modality. CQCA is a novel sequential mixed-method technique [42] for analyzing qualitative data in a quantitative contrastive manner that capitalizes on the unique benefits of combined quantitative and qualitative analyses. CQCA has been used successfully in various studies to examine patterns in public attitudes and perceptions [37].

Within the entire pooled sample of 3,603 participants, 452 entered either no response or one unrelated to the question. This resulted in a final analyzed sample of 3,151 responses. To reduce researcher bias, we randomized this full set of responses and blinded coders to each participant's experimental condition. We then performed a conventional content analysis of the blinded responses, identifying themes inductively in an iterative approach. Table OR10 in the Online Resources file displays our final coding scheme (containing six broad categories of themes) and the percentages of all 3,151 responses featuring each theme.

<sup>1</sup> Table OR2 in the Online Resources file has links to all video-vignettes.

We dichotomously coded each response for the presence (1) or absence (0) of each theme. Thus, a given response may contain more than one theme.

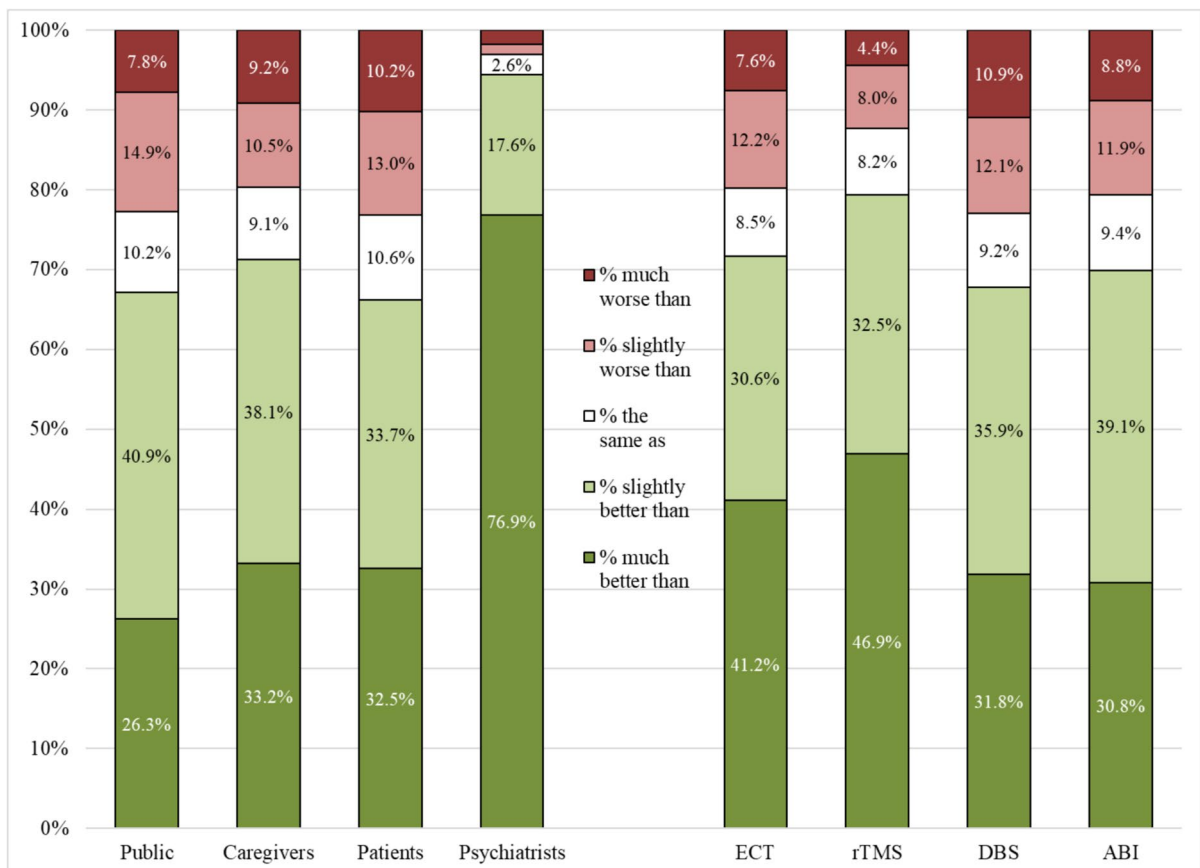
After unblinding this qualitative data, we performed a series of one-way ANOVA tests with Tukey's HSD tests to examine variation in the percentages of key themes across stakeholder group, assigned PEI modality, and responses to the closed-ended survey question above. Below we present results for those four categories of themes that appeared in at least 25% of all responses: negative attitudes toward depression and positive, cautionary, and negative attitudes toward assigned PEI modality. Tables OR13 and OR14 and Figure OR1 in the Online Resources file contain the results for the remaining two categories of themes that appeared in less than 25% of all responses: references to other interventions and barriers to PEI use. Within these

general categories, we focus exclusively on specific themes that appeared in at least 5% of all responses.

## Results

### Participants' Perception of How Their Assigned PEI Compares to Living with TRD

A large majority of participants (72.1%) reported that their assigned PEI was better than living with TRD (37.5% much better than; 34.6% slightly better than). A small percentage (19.1%) reported that their assigned PEI was worse than living with TRD (8.0% much worse than; 11.1% slightly worse than). An even smaller percentage (8.9%) reported that their assigned PEI was the same as living with TRD. Yet, these overall percentages mask ample variation in



**Fig. 1** Percentage of Participants Reporting How Treatment Compares to Living with Treatment-Resistant Depression by Stakeholder Group and Assigned PEI Modality

percentages by stakeholder group and assigned PEI modality, which are displayed in Fig. 1.

While 68.3% of non-clinicians (67.2% of general public, 71.2% of caregivers, and 66.2% of patients) perceived their assigned PEI to be better than living with TRD, approximately 94.4% of psychiatrists reported such a favorable assessment. A one-way ANOVA revealed a statistically significant effect of stakeholder group on the comparison between assigned PEI and living with TRD:  $F(3, 3147) = 89.53$ ,  $p < 0.001$ . The effect size, eta squared ( $\eta^2$ ), is 0.08, indicating a medium effect. While 71.7% of participants in the ECT condition, 67.8% of participants in the DBS condition, and 69.9% of participants in the ABI condition perceived their assigned PEI to be better than living with TRD, 79.4% of participants assigned to the rTMS condition reported such a favorable assessment. A one-way ANOVA revealed a statistically significant effect of assigned PEI modality on the

comparison between assigned PEI and living with TRD:  $F(3, 3147) = 18.78$ ,  $p < 0.001$ . The  $\eta^2$  is 0.02, indicating a small effect.

### Participants' Negative Attitudes about Depression

Approximately 38% of participants' responses communicated negative attitudes toward depression, with two themes appearing in at least 5% of all responses: *general negative affect toward depression* and *untreated depression can be very dangerous*. Table 1 below presents illustrative examples of these two themes as well as the percentages of stakeholder groups and PEI modality conditions featuring each theme. In this and similar tables, we identify the source of each illustrative example by their stakeholder group and their response to the question comparing their assigned PEI modality with TRD.

Approximately 33.8% of responses expressed negative affect toward depression in general,

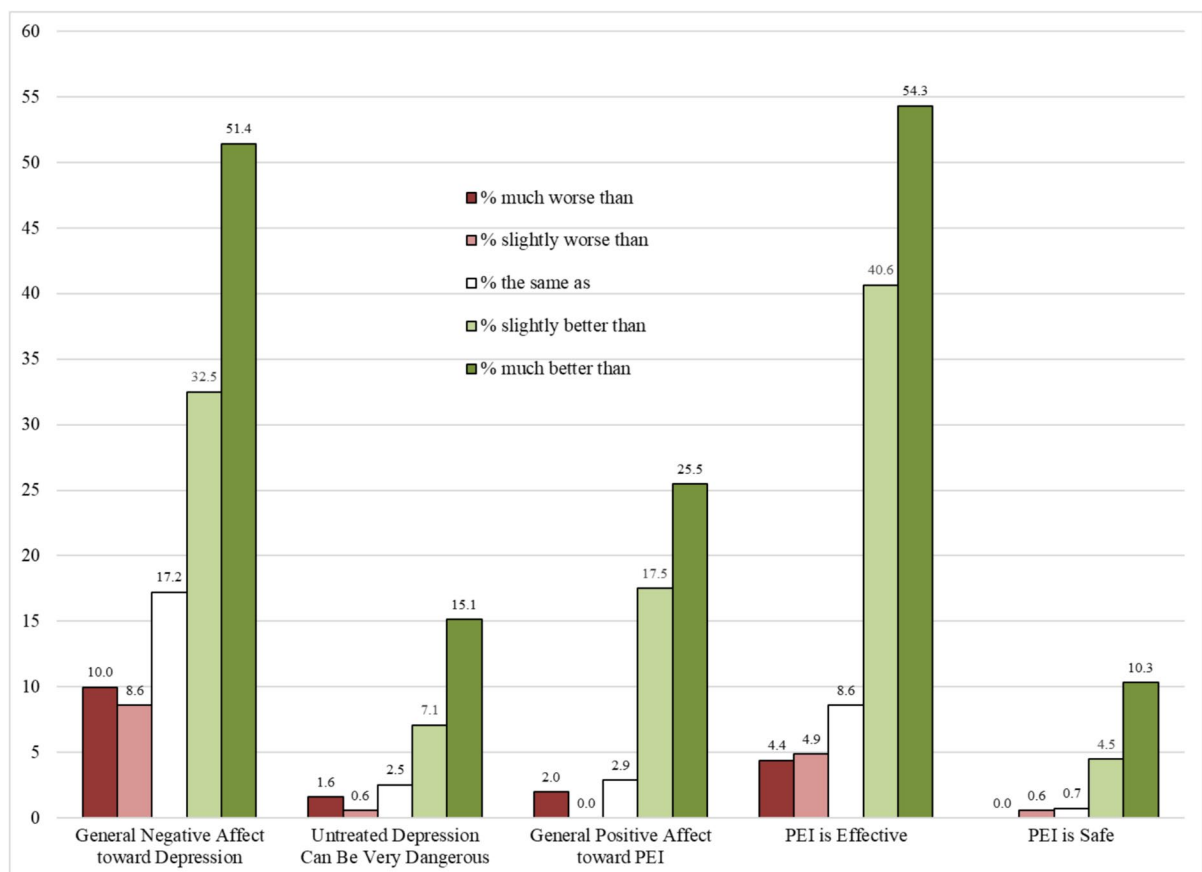
**Table 1** Percentages of negative attitude toward depression themes in responses by stakeholder group and assigned PEI modality

Theme	Illustrative Example(s) (Stakeholder Group, PEI Comparison to Life with TRD)	Group	% of Responses	F-Test (3, 3147)
General Negative Affect toward Depression	"I believe ECT is probably worth a try, if nothing else then as a last-ditch effort. Depression is debilitating and it can destroy a person's self-worth and willingness to live. It is worth trying any relatively safe therapy that may break this cycle." (Patient, ECT much better than TRD)	Public	28.4%	$F = 18.98$ $p < 0.001$ $\eta^2 = 0.02$
		Caregivers	31.4%	
		Patients	34.2%	
		Psychiatrists	48.0%	
	"When your depression is so bad that you have no energy to do anything and all you think about is wanting to just quit existing, this sounds like a viable solution. They have used electrical brain stimulation for other conditions for years, so the science is not untested. The side effects of most antidepressants are also no picnic. It is very frustrating to be on the medicine-go-round trying to find which one might work for you." (Caregiver, ABI much better than TRD)	ECT	33.1%	$F = 5.93$ $p < 0.001$ $\eta^2 = 0.01$
		rTMS	40.0%	
		DBS	30.9%	
		ABI	31.6%	
Untreated Depression Can Be Very Dangerous	"Severe depression negatively affects every aspect of your life: self-esteem, daily functioning, hygiene, socializing, sleep, and the ability to work. Not only that, a losing battle can end with suicide." (Patient, ECT much better than TRD)	Public	6.6%	$F = 14.78$ $p < 0.001$ $\eta^2 = 0.01$
		Caregivers	8.7%	
		Patients	6.3%	
		Psychiatrists	16.1%	
	"TRD is one of the worst and most painful afflictions that humans suffer. Receiving TMS while time-consuming, may be a slight annoyance to a patient. However, TRD may kill a patient." (Psychiatrist, rTMS much better than TRD)	ECT	9.7%	$F = 0.95$ $p = 0.42$ $\eta^2 = 0.00$
		rTMS	8.1%	
		DBS	8.9%	
		ABI	7.5%	
	"If the pros outweigh the cons, then I can't see the reason to not try TMS. More severe forms of depression can be fatal, so at least trying it seems to be worth a shot." (Public, rTMS much better than TRD)			

and 8.5% of responses expressed the sentiment that untreated depression can be very dangerous. Greater percentages of psychiatrists than non-clinicians expressed each of these themes. A greater percentage of participants in the rTMS condition than in the other three PEI conditions communicated negative affect toward depression; however, prevalence of this second theme did not vary significantly by PEI modality. The first two clusters in Fig. 2 below display the percentages of participants reporting either of these two negative attitude themes by their comparison of their assigned PEI to living with TRD. As expected, much greater percentages of participants who assessed their assigned PEI as better than living with TRD reported these two themes than did their counterparts who assessed their assigned PEI as worse than living with TRD.

### Participants' Positive, Cautionary, and Negative Attitudes toward Assigned PEI

Approximately 51% of participants' responses communicated positive attitudes toward their assigned PEI, with three themes appearing in at least 5% of all responses: *general positive affect toward assigned PEI* (16.0%), *PEI is effective* (36.1%), and *PEI is safe* (5.6%). Table 2 below presents illustrative examples of these three themes. A lesser percentage of the general public than of the other three stakeholder groups expressed general positive affect toward their assigned PEI, while PEI modality was not associated with the prevalence of this theme. Greater percentages of psychiatrists than of non-clinicians commented that their assigned PEI was effective and safe. A lesser percentage of patients and those in the DBS condition than their respective



**Fig. 2** Percentages of Participants Reporting Negative Attitude toward Depression Themes and Positive Attitude toward Assigned PEI Themes by Perceived Comparison of Their Assigned PEI with TRD



**Table 2** Percentages of positive attitude toward PEI themes in responses by stakeholder group and assigned PEI modality

Theme	Illustrative Example(s) (Stakeholder Group, PEI Comparison to Life with TRD)	Group	% of Responses	F-Test (3, 3147)
General Positive Affect toward PEI	“I personally would rather try this treatment then have to take daily medication.” <i>(Patient, ECT much better than TRD)</i> “I think it would be slightly better because it would be targeting the direct areas of the brain responsible for depression. This might be more enjoyable because there’s no more need for antidepressants.” <i>(Public, ABI slightly better than TRD)</i> “If this new treatment meant not being so depressed and not having to take an anti- depression medication for the rest of your life, it has to be a better alternative.” <i>(Public, rTMS much better than TRD)</i>	Public	12.0%	F = 5.42
		Caregivers	18.5%	$p = 0.001$
		Patients	17.2%	$\eta^2 = 0.01$
		Psychiatrists	16.9%	
		ECT	16.0%	F = 0.89
		rTMS	17.8%	$p = 0.44$
		DBS	14.9%	$\eta^2 = 0.00$
		ABI	15.5%	
PEI Is Effective	“I am an ECT provider. ECT is more efficacious overall, and much quicker to act, compared to any other treatment of depression. ECT is safe in well selected patients.” <i>(Psychiatrist, ECT much better than TRD)</i> “In my opinion, getting some form of treatment when you have reached the end of the line and start wanting to end everything is better than doing nothing and letting the worst happen.” <i>(Caregiver, rTMS slightly better than TRD)</i> “I believe ABI seems much better than living with treatment-resistant depression because this has a huge chance to work. ... I think it is worth the shot for a happy life.” <i>(Public, ABI much better than TRD)</i>	Public	36.8%	F = 8.08
		Caregivers	37.2%	$p < 0.001$
		Patients	30.4%	$\eta^2 = 0.01$
		Psychiatrists	43.5%	
		ECT	37.9%	F = 2.45
		rTMS	38.6%	$p = 0.06$
		DBS	32.7%	$\eta^2 = 0.00$
		ABI	35.2%	
PEI is Safe	“ECT can be a safe, effective, and rather quick treatment for TRD. Yes, there are potential side effects, which medications also have.” <i>(Psychiatrist, ECT much better than TRD)</i> “rTMS is not as rapid acting as ECT but has far fewer side effects than ECT and medications. rTMS requires a daily commitment to treatment that is greater than taking meds and more frequent than ECT. But, the intrusiveness of rTMS into a person’s life is far less than the malignant disruption caused by TRD.” <i>(Psychiatrist, rTMS much better than TRD)</i> “[PEI] is safe, effective and the closest I ever get to a miracle in my practice. For the right patient, it is Heaven’s gift.” <i>(Psychiatrist, ECT much better than TRD)</i>	Public	2.6%	F = 51.13
		Caregivers	5.1%	$p < 0.001$
		Patients	2.9%	$\eta^2 = 0.05$
		Psychiatrists	17.1%	
		ECT	7.2%	F = 6.99
		rTMS	7.7%	$p < 0.001$
		DBS	3.9%	$\eta^2 = 0.01$
		ABI	3.6%	

counterparts noted their assigned PEI’s effectiveness. Also, greater percentages of participants in the ECT and rTMS conditions than in the DBS or ABI (i.e., implantable) conditions discussed the safety of their assigned PEI.

The last three clusters in Fig. 2 above display the percentages of participants reporting any of these three positive attitude themes by their comparison of their assigned PEI to living with TRD. As expected, much greater percentages of participants who assessed their assigned PEI as better than living with TRD reported these three themes than did

their counterparts who assessed their assigned PEI as worse than living with TRD.

Approximately 38% of participants’ responses communicated cautionary attitudes toward their assigned PEI, with four themes appearing in at least 5% of all responses: *uncertainty about PEI effectiveness* (17.2%), *perceived lack of information to support PEI use* (12.0%), *PEI is invasive* (11.2%), and *PEI as a last resort* (5.2%). Table 3 below presents illustrative examples of these four themes. A greater percentage of psychiatrists than of non-clinicians included one of these four cautionary themes in their

**Table 3** Percentages of cautionary attitude toward PEI themes in responses by stakeholder group and assigned PEI modality

Theme	Illustrative Example(s) (Stakeholder Group, PEI Comparison to Life with TRD)	Group	% of Responses	F-Test (3, 3147)
Uncertainty about PEI Effectiveness	<p>“ECT in my opinion sounds interesting, fascinating even in the since that this is how far humans have come with medical and scientific advances. The idea of rewiring your brain so to speak seems to make sense from what I understand about how emotions work in your brain. However with all of that being said, it does also sound quite invasive and with that a bit scary.” (Patient, ECT slightly better than TRD)</p> <p>“Effective treatment of TRD is much better than not treating it. ECT can sometimes be very effective. However, we cannot be 100% predictive on who will get great benefit, partial benefit, or little if any benefit. That’s the real dilemma. ... Given the risk benefit ratio, I would prefer to start with TMS.” (Psychiatrist, ECT much better than TRD)</p>	Public	15.5%	F = 21.31 $p < 0.001$ $\eta^2 = 0.02$
		Caregivers	14.9%	
		Patients	14.6%	
		Psychiatrists	30.0%	F = 0.80 $p = 0.49$ $\eta^2 = 0.00$
		ECT	17.6%	
		rTMS	18.7%	
		DBS	16.9%	
		ABI	15.8%	
Perceived Lack of Information to Support PEI Use	<p>“I would like to better understand the risks involved with ECT, including long term plan that involves psychotherapy. Overall, it could be a promising option for a disorder that eludes effective treatment in any other way.” (Caregiver, ECT much better than TRD)</p> <p>“I don’t know enough about it to be confident.” (Public, rTMS slightly better than TRD)</p> <p>“The side effects seem extreme and scary. While depression sucks and some antidepressants can have major side effects, the unknowns about this procedure seem more fearful and uncertain.” (Public, DBS the same as TRD)</p>	Public	10.5%	F = 6.62 $p < 0.001$ $\eta^2 = 0.01$
		Caregivers	10.5%	
		Patients	11.8%	
		Psychiatrists	18.0%	F = 3.29 $p = 0.02$ $\eta^2 = 0.00$
		ECT	9.6%	
		rTMS	14.5%	
		DBS	12.8%	
		ABI	11.1%	
PEI is Invasive	<p>“While it’s a more reputable way of helping with depression I’m concerned about how invasive it can be for a person.” (Public, rTMS slightly better than TRD)</p> <p>“I’d really have to understand more about the use of this new technology. It seems more invasive than medications, but perhaps less impactful. It could potentially be a game-changer for certain people if they are willing to live with an implant for the rest of their lives.” (Caregiver, ABI slightly better than TRD)</p> <p>“It sounds very invasive to have something put into the brain and having to frequently undergo surgery for this. Too science fiction.” (Patient, DBS slightly worse than TRD)</p>	Public	10.4%	F = 10.14 $p < 0.001$ $\eta^2 = 0.01$
		Caregivers	8.8%	
		Patients	10.7%	
		Psychiatrists	18.4%	F = 26.37 $p < 0.001$ $\eta^2 = 0.03$
		ECT	5.8%	
		rTMS	6.6%	
		DBS	16.6%	
		ABI	15.6%	



**Table 3** (continued)

Theme	Illustrative Example(s) (Stakeholder Group, PEI Comparison to Life with TRD)	Group	% of Responses	F-Test (3, 3147)
PEI as Last Resort	“As a person who suffers from depression and anxiety, this would be an absolute last resort for me as it is so invasive. But I would be willing to try if I had to.” (Patient, ECT slightly better than TRD)	Public	5.9%	F=9.95 $p<0.001$ $\eta^2=0.01$
		Caregivers	3.5%	
		Patients	3.8%	
		Psychiatrists	9.9%	
	“Surgery is bad enough, brain surgery is scary and dangerous. I’d try 1000 different pills before I did anything surgical.” (Patient, DBS the same as TRD)	ECT	4.9%	F=0.22 $p=0.88$ $\eta^2=0.00$
		rTMS	5.0%	
		DBS	5.8%	
		ABI	5.2%	
	(Caregiver, rTMS much better than TRD)			

response. PEI modality was not associated with the prevalence of the first and fourth cautionary themes. Compared to those participants in the ECT condition, a greater percentage in the rTMS condition noted a perceived lack of data or information to support use of their assigned PEI. Also, greater percentages of participants assigned to the implantable conditions than those assigned to the ECT or rTMS conditions reported concerns with their assigned PEI’s invasiveness.

The first four clusters in Fig. 3 below display the percentages of participants reporting each of these four cautionary attitude themes by their comparison of their assigned PEI to living with TRD. Greater percentages of participants who assessed their assigned PEI as better than living with TRD reported uncertainty about the effectiveness of their assigned PEI, and greater percentages of participants who assessed their assigned PEI as worse than living with TRD characterized their assigned PEI as invasive. Also, greater percentages of participants which assessed their assigned PEI as the same as living with TRD noted a perceived lack of information available to support its use.

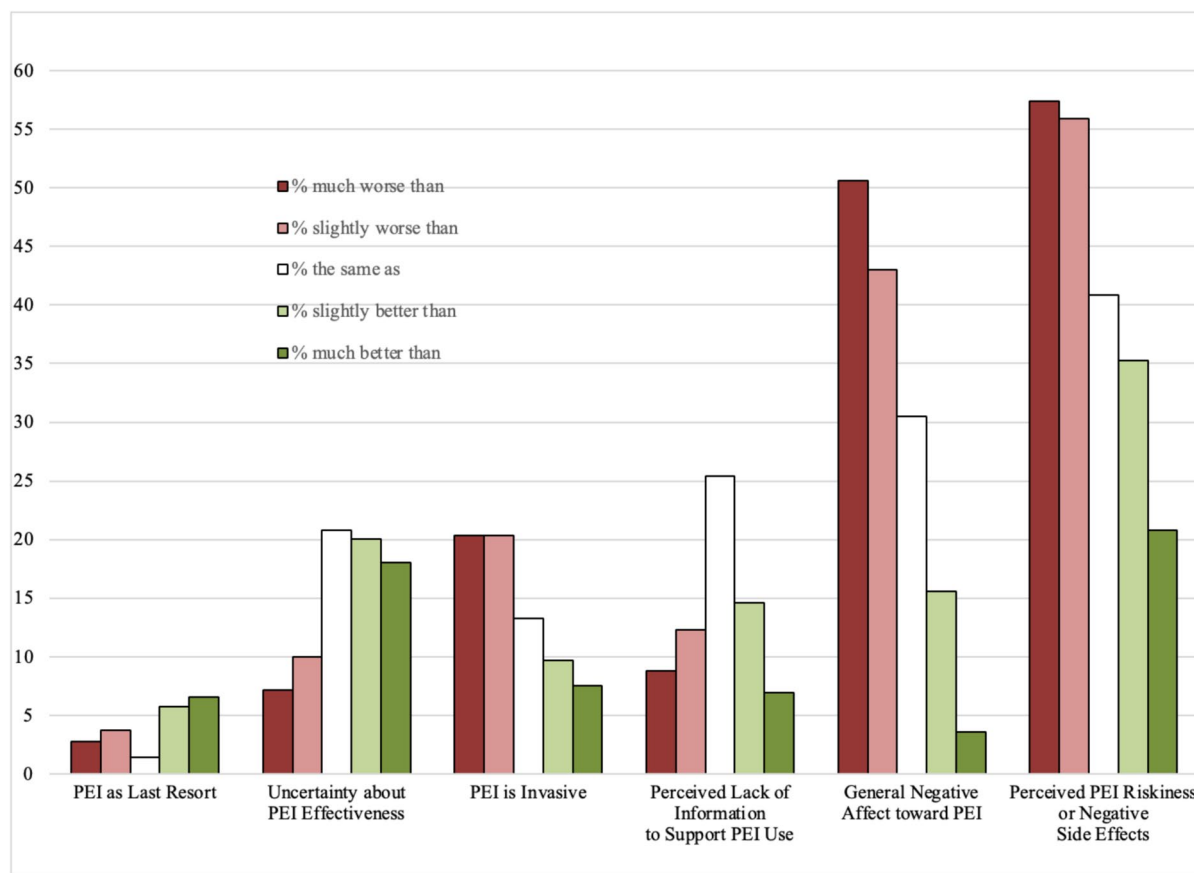
Approximately 45% of participants’ responses communicated negative attitudes toward their assigned PEI, with two themes appearing in at least 5% of all responses: *general negative affect toward PEI* (18.2%) and *perceived PEI riskiness or negative side effects* (34.4%). Table 4 below presents illustrative examples of these two themes. Greater percentages of non-clinicians than of psychiatrists included

one of these two negative themes in their response. Lesser percentages of those in the rTMS condition than in the other three PEI conditions included one of these two negative themes in their response.

The last two clusters in Fig. 3 above display the percentages of participants reporting each of these two negative attitude themes by their comparison of their assigned PEI to living with TRD. Greater percentages of participants who assessed their assigned PEI as worse than living with TRD reported these two negative attitude themes than did participants who assessed their assigned PEI as better than living with TRD.

## Discussion

Approximately 72% of all participants reported that receiving their assigned PEI would be better than living with TRD, and their explanations for this favorable assessment contained a range of themes. Among these, participants predominantly expressed negative feelings about depression and positive feelings about their assigned PEI; further, they especially perceived untreated depression to be very dangerous and their assigned PEI modality to be effective and safe. Approximately 20% of all participants reported that receiving their assigned PEI would be worse than living with TRD, and they especially explained this unfavorable assessment by expressing negative feelings about their assigned PEI and by noting that it is invasive, is risky, or has negative side effects. The



**Fig. 3** Percentages of Participants Reporting Cautionary or Negative Attitude toward Assigned PEI Themes by Perceived Comparison of Their Assigned PEI with TRD

prevalence of many themes differed substantially by stakeholder group—with psychiatrists typically offering different reasons for their assessment than non-clinicians—but much less so by PEI modality. In some ways, this clinician/non-clinician divide in views parallels the long-time divide in risk perceptions among experts/analysts and laypeople in approximately 50 years of social science research. One main takeaway from this latter literature is that much of this divide is due to laypeople considering a wider array of factors in their assessment of the riskiness of a technology/event/behavior (e.g., dread, perceived lack of control, overall uncertainty, delay between action and consequence, emotional imagery, etc.)—largely via intuitive biases and cognitive heuristics—than the narrower criteria considered by technical experts (e.g., probability of adverse outcome X magnitude of consequences of the adverse outcome). We interpret

these findings here, noting where they differ across stakeholder groups and/or PEI modalities.

#### Negative Attitudes toward Depression

Approximately 38% of participants offered negative comments about living with depression, with a greater percentage of these coming from participants who assessed their assigned PEI as better than living with TRD. Psychiatrists especially expressed negative affect toward TRD and noted how very dangerous untreated depression can be. To a lesser extent, non-clinicians also commented on the difficulty of life with depression and the pervasive effects of depression on the lives of patients and their families and friends. These attitudes may reflect broader changes in public attitudes toward depression over the past few decades, as stigmatizing beliefs about depression

**Table 4** Percentages of negative attitude toward PEI themes in responses by stakeholder group and assigned PEI modality

Theme	Illustrative Example(s) (Stakeholder Group, PEI Comparison to Life with TRD)	Group	% of Responses	F-Test (3, 3147)
General Negative Affect toward PEI	“It seems scary and somewhat barbaric, but it 100% seems much better than the alternative of living like that.” <i>(Patient, ECT much better than TRD)</i> “Seems like it could be potentially dangerous and do more harm than good in the long run. Doesn’t seem too safe.” <i>(Patient, rTMS slightly worse than TRD)</i> “The very idea is inhumane and due to the electrical component it could lead to seizures, bleeding of the brain, possibly death. I see the risks greatly outweighing the benefits.” <i>(Patient, DBS slightly worse than TRD)</i> “You are being controlled like a robot.” <i>(Patient, DBS slightly worse than TRD)</i>	Public	18.1%	F = 35.80 $p < 0.001$ $\eta^2 = 0.03$
		Caregivers	19.1%	
		Patients	25.4%	
		Psychiatrists	3.0%	F = 6.47 $p < 0.001$ $\eta^2 = 0.01$
		ECT	21.7%	
		rTMS	13.3%	
		DBS	18.5%	
		ABI	19.1%	
Perceived PEI Riskiness or Negative Side Effects	“The potential benefits of DBS for treating TRD are great, but it requires invasive surgery in the brain with many potential complications. Living with some of the complications would be far worse than living with TRD.” <i>(Psychiatrist, DBS slightly better than TRD)</i> “I would be worried every day that something would go wrong within the electrical system.” <i>(Public, DBS slightly worse than TRD)</i> “I love how innovative technology is; I’m sure someday humans will have technological implants. However, I’m not comfortable implanting a technology in the brain. Seems way too risky.” <i>(Public, ABI slightly worse than TRD)</i>	Public	37.0%	F = 4.31 $p = 0.005$ $\eta^2 = 0.00$
		Caregivers	36.6%	
		Patients	32.4%	
		Psychiatrists	28.7%	F = 18.56 $p < 0.001$ $\eta^2 = 0.02$
		ECT	34.7%	
		rTMS	23.8%	
		DBS	40.3%	
		ABI	38.1%	

have decreased somewhat [43], perhaps in part due to widespread anti-stigma campaigns [44]. There also has been an increasing acceptance of biological causes of [45], and biological treatments for [46], depression. Overall, regardless of their assessment of their assigned PEIs, participants recognized TRD as a serious and debilitating condition.

#### Positive, Cautionary, and Negative Attitudes toward Assigned PEI

Even though 72% of participants assessed their assigned PEI as better than living with TRD, only about half of all participants expressed a clearly positive sentiment toward this treatment. This suggests that participants’ favorable assessment of their

assigned PEI may have been driven just as much by their negative views of depression as their positive views of their assigned treatment. Further, favorable assessments also were provided, though in smaller percentages, by participants who volunteered cautionary and even negative sentiments toward their assigned PEI. This suggests that participants’ views of their assigned PEIs are nuanced and textured—far from either openly embracing or opening dismissive.

While about 36% of participants commented on the effectiveness of their assigned PEI; 17% expressed uncertainty about this effectiveness; another 12% reported not knowing how their assigned PEI works, not having data to support its use, and/or not knowing about its long-term effectiveness [47]; and about 5% acknowledged the acceptability of their

assigned PEI as a last resort. Psychiatrists were more likely than non-clinicians to mention each of these seemingly contradictory themes. This likely reflects the salience of treatment effectiveness among psychiatrists combined with their general unwillingness to speculate on those treatments of which they have little or no professional knowledge [48]. Further, we crafted the vignettes to minimize differences in how we described the four PEI modalities (to optimize the experiment's internal validity). As such, the vignettes did not mention that DBS or ABIs are experimental therapies, something of which psychiatrists likely were aware. This may have influenced their responses about uncertainty and/or lack of knowledge.

Front-line treatments for TRD include antidepressant medications and psychotherapy. Currently approved PEIs tend to be used only when patients do not respond to these treatments. Tempered expressions of treatment effectiveness (i.e., that it would be “worth a try”) and perceiving a treatment as acceptable “as a last resort” seem reasonable in this regard, and they also are consistent with recent scholarship on stakeholders' views. Cabrera et al. [49] find that many members of the public participating in focus groups viewed psychiatric surgery (including DBS) as a treatment of last resort. While Lutchman et al. [50] find that psychiatrists viewed ECT as a treatment of last resort, Cabrera et al. [48] more recently find that psychiatrists reported differing views on when ECT should be considered in the overall course of treatment.

Approximately 34% of participants expressed concerns about the riskiness or negative side effects of their assigned PEI. Among those who assessed treatment with their assigned PEI as better than living with TRD, relatively few described it as safe or as only having minimal side effects. Rather, they acknowledged the risks and side effects associated with treatment and reported that the treatment benefits outweigh these risks. In contrast, over half of those participants who assessed their assigned PEI as worse than living with TRD emphasized that the risks and side effects associated with the treatment were serious. Such concerns about risks and side effects tended to co-occur with other themes such as general negative feelings toward their assigned PEI. Further, participants assessing their assigned PEI as worse than living with TRD more often considered their treatment to be invasive and expressed opposition to

any intervention into the brain. Similarly, interviewing psychiatric inpatients with TRD about their interest in and concern about receiving DBS, Lawrence et al. [51] finds that many of them expressed concerns about the risks of the procedure and that some explicitly disliked the invasive nature of DBS.

The prevalence of comments about treatment safety and invasiveness varied by PEI modality. Greater percentages of participants assigned to the ECT and rTMS conditions perceived their assigned treatment as safe and non-invasive than did those assigned to the implantable conditions (i.e., DBS and ABIs). This aligns with a traditional (physical) conceptualization of invasiveness as involving breaking the skin, removing something from inside the body, or inserting something into the body. Compared to their counterparts in the ECT and rTMS conditions, participants in the implantable conditions more often perceived their assigned PEI as risky with negative side effects (likely because these treatments require surgery) and more often expressed general opposition to *any* intervention into the brain. This suggests that perceived invasiveness and worry about harm potential go hand-in-hand ([52], see also [53]), and that this relationship may be stronger with the increasing “directness” of the PEI's effects on the brain [54–57]. Also, recent work by Bluhm et al. [52] suggests stakeholders' likely lesser familiarity with implantables also may have influenced their more negative sentiments toward these treatments.

Those in the rTMS condition reported the fewest generally negative attitudes or concerns about risks of all four PEI modality conditions. rTMS does appear to be relatively low-risk compared to other neuromodulation treatments [5, 6]. Further, although earlier protocols required multiple sessions per week for a number of weeks, shorter courses of treatment developed more recently are showing promise [58]. Likely adopting the traditional view of invasiveness noted above, most experts frequently describe rTMS as a non-invasive form of neurostimulation [59–61]—even as other experts dispute this characterization [54, 62], noting that the effects of rTMS spread beyond the specific site of stimulation.

Finally, in recent years the neuroethics literature has featured myriad discussions about potentially negative changes to the self-related characteristics (e.g., personality, identity, autonomy) of patients receiving neurostimulation—especially among those

being treated with DBS (usually for Parkinson's disease) [17, 18, 63]. Recent studies analyzing data from interviews about PEI therapies with selected stakeholder groups do find that stakeholders express concerns about negative changes to self but also are likely to mention positive changes to the self with such treatments [18, 20, 48, 57, 64]. Nevertheless, as documented in Table OR2 in our Online Resources file, very few participants in our study referenced any types of PEI-induced changes to self-related characteristics. Approximately 2.1% noted that their assigned PEI may change self-related characteristics in a negative way, while 0.4% claimed their assigned PEI may change self-related characteristics in a positive way.

### Limitations

This study has a few limitations. First, for conceptual and theoretical reasons, we only focused on four PEIs. Future work will be needed to further examine how technological features and other factors might raise different ethical concerns for other novel electroceuticals. Second, we only focused on the use of PEIs for treating TRD. As such, these results likely are not applicable to other psychiatric disorders for which PEIs might be used. Moreover, we recognize that the four interventions we compared vary in their current approval status for clinical use and the level of TRD a patient must exhibit to be a candidate for them. These factors may have influenced participants' responses, even though random assignment should have neutralized this influence across experimental conditions. We developed the hypothetical scenario in our video vignettes to provide an equivalent point of comparison (and thus optimize experimental internal validity), even further mitigating this influence which helped us achieve our aim of anticipating potential ethical concerns with these interventions beyond those associated only with their current use. Third, with their greater knowledge of TRD and psychotherapy, psychiatrists and/or patients with severe depression may have judged the video vignettes as less realistic than did caregivers and members of the general public. Fourth, we relied upon a single-item measure to capture participants' assessment of their assigned PEI relative to living with TRD. While creating a multiple-item scale for this purpose might have improved this measure, our follow-up

open-ended question nevertheless provided participants an opportunity to elaborate freely on their often nuanced views.

### Conclusion

Investigating relevant stakeholders' assessments of whether a treatment is worse than its targeted disease turned out to be a complex endeavor. Their assessments reflected not just their attitudes and concerns about their assigned PEI modality, but also their beliefs and attitudes about the treatment-resistant depression the therapy aims to ameliorate. Each PEI modality examined in this study has its own developmental trajectory, unique characteristics, and a distinct risk–benefit profile. Further, these characteristics and profiles for newer PEI modalities are changing as we learn more about their emerging applications for depression.

Our results highlighted not only differences between psychiatrists and non-clinicians but also between implantable and non-implantable electroceuticals. Some of these differences are likely shaped the psychiatrist evidence base knowledge of these interventions compared to the non-clinician participants, a large gap in mental health literacy and the likely greater influence of stigma (about both the disorder and treatments) among laypeople. These results also reflect an important legacy of perceptions about the use of electricity in the body and of direct intervention into the brain. The richness of the narrative responses to our open-ended question enabled us to put in context and add depth to key patterns seen in recent survey-based research on PEIs. Nevertheless, more research is needed to continue improving our scientific understanding of how different socio-cultural factors and values influence relevant stakeholders' views about these important kinds of treatments for depression. Further, psychiatric professionals, neuromodulation technology developers, and mental health advocates must continue working to dispel unfounded concerns about, and reduce hype about potential benefits of, using PEIs for treating depression.

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**Data Availability** The dataset used and analysed during the current study is available from the research team on reasonable request (lcabrera@psu.edu or mccright@msu.edu). Once we have completed analysis of the full dataset from which this paper is part of, we will post the direct links to the data repositories to <https://peiproject.com/>.

## Declarations

**Competing Interests** LC, RB, and AM have no conflicts of interest to declare. EA has received research support from the following entities in the preceding 12 months: Alkermes, Boehringer-Ingelheim, Janssen, Karuna, Neurocrine Biosciences, Teva, and the Vanguard Research Group. EA also has served on advisory boards or consulted with Alkermes, Boehringer-Ingelheim, Clinical Care Options, CMEology, CME Outfitters, and VML Health.

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