

PAPER

# Understanding, interests and informed consent: a reply to Sreenivasan

Danielle Bromwich

**Correspondence to**

Dr Danielle Bromwich,  
Department of Philosophy,  
University of Massachusetts,  
Boston, Wheatley Hall,  
5th Floor, Rm 10, Boston, MA  
02125, USA;  
[daniellebromwich@gmail.com](mailto:daniellebromwich@gmail.com)

Received 28 March 2013

Revised 27 November 2013

Accepted 2 April 2014

**ABSTRACT**

It is widely agreed that the view of informed consent found in the regulations and guidelines struggles to keep pace with the ever-advancing enterprise of human subjects research. Over the last 10 years, there have been serious attempts to rethink informed consent so that it conforms to our considered judgments about cases where we are confident valid consent has been given. These arguments are influenced by an argument from Gopal Sreenivasan, which apparently shows that a potential participant's consent to research participation can be perfectly valid even if she fails to understand the risk-benefit profile of the study. I argue that Sreenivasan's argument fails. The set of clinical trials that is supposed to be ethical in the face of this kind of ignorance is empty. However, I argue that his argument is nonetheless instructive in allowing us to identify three important but neglected areas for future conceptual research on informed consent. I close by arguing that research on these identified questions promises to yield a defensible view of consent, lessen the burden of ambiguity on researchers attempting to obtain consent to research participation, and facilitate socially valuable research.

**INTRODUCTION**

Some think that informed consent has received too much scholarly attention in research ethics.<sup>1-3</sup> It is not a necessary condition of ethical medical research, and regulatory oversight protects against the kind of coercion and deception that clearly invalidates consent.<sup>4</sup> Yet despite the attention it has received, significant problems remain that require resolution.

Nearly 30 years have passed since the first studies were published on the therapeutic misconception showing that many patient participants confuse the aims of clinical research with the aims of clinical care.<sup>5</sup> Since then, a wide range of studies show that many otherwise competent adults fail to adequately understand what is disclosed to them about the research that they have enrolled in.<sup>6-7</sup> The standard view of informed consent tells us that adequate understanding of what is disclosed is a necessary condition of valid consent to medical research participation.<sup>8-12</sup> But when this view is taken together with the studies on poor participant comprehension, it implies that many otherwise unproblematic trials are, in fact, unethical since researchers failed to obtain valid consent to medical research participation that morally required it. This is a surprising conclusion. If we think that many of these trials are

still ethical, we must revisit the standard view of informed consent.

More recently, the move to calibrate the rigours of the consent process to the risks of the research also demonstrates the need for a more systematic analysis of informed consent. Many scholars and regulators worry that researchers are excessively burdened, and that socially valuable research is impeded by the over-regulation of low-risk research.<sup>13-14</sup> But appropriately modernising the current regulations for obtaining valid consent to medical research participation involves more than merely paying attention to the risks of the study; it requires a proper understanding of the purpose of consent and the protection it offers. A defensible and appropriately risk-adapted approach to informed consent, for example, would need to work out how the process can be attentive to the risks of the research without attenuating the quality of the consent obtained.

These problems alone suggest that the view of informed consent found in the regulations and guidelines struggles to keep pace with the ever-advancing enterprise of human subjects research. But rather than give up on what some think is a 'culturally biased, legalistic, ritualistic and unevenly enforced'<sup>15</sup> practice, these problems give us the opportunity to reflect upon its purpose and revise it so that it conforms to our considered judgments about cases where we are confident valid consent has been given. Over the last 10 years, there have been several serious attempts to do just this.<sup>16-19</sup> These attempts are all influenced by an argument from Gopal Sreenivasan. He argues that a potential participant's consent to research participation can be perfectly valid even if she fails to understand the risk-benefit profile of the study. Many think that the value of Sreenivasan's argument lies in this result: he supposedly shows that some clinical trials are ethical in the face of known misconception. In what follows, I argue that Sreenivasan's argument fails. The set of clinical trials that is supposed to be ethical in the face of this kind of ignorance or misconception is empty. I argue that the value of Sreenivasan's argument lies in a distinction he makes between the purpose of the informational requirements for informed consent: the disclosure and understanding requirements. This distinction allows us to identify three important but neglected areas for future research on informed consent to medical research participation.

**SREENIVASAN'S ARGUMENT**

Sreenivasan's argument starts from the expected moral cost of enforcing the standard view of

**To cite:** Bromwich D. *J Med Ethics* Published Online First: [please include Day Month Year] doi:10.1136/medethics-2013-101499

informed consent's understanding requirement in light of the prevalence of poor participant comprehension of what is disclosed.<sup>16 20</sup> He writes:

...given the difficulty in achieving adequate comprehension of the standard disclosure in a suitable number of prospective subjects, a predictable consequence of enforcing a requirement of adequate comprehension will be to imperil clinical research of considerable moral value and importance. Hence, our *justification* for this requirement had better be pretty impressive, so as to warrant a moral cost of that magnitude.<sup>20</sup>

One plausible justification runs as follows. The requirement of adequate comprehension gives prospective participants the opportunity to protect their interests. When in the grips of the therapeutic misconception, patient participants frequently fail to grasp a trial's true risk-benefit ratio. In failing to adequately understand this aspect of the research, they are not well placed to protect their interests. However, Sreenivasan argues that there is a set of trials that is ethically unaffected by ignorance of this sort.

The trials that Sreenivasan has in mind are those that pass research ethics committee (REC) review, comply with the regulations, are beyond Phase I testing and have a favourable risk-direct benefit ratio. This is a ratio that remains favourable 'even when direct benefit to the participant is the only benefit taken into account'.<sup>16</sup> When a competent adult voluntarily agrees to participate in such a trial after receiving relevant information about the research, Sreenivasan claims that her consent is 'perfectly valid'<sup>16</sup> even if she is ignorant of the trial's true risk-benefit ratio. He derives this claim from a purpose that is served by the understanding requirement for valid informed consent: it affords a prospective participant the opportunity to protect her interests by grasping exactly what she is authorising. However, when a trial is properly and independently assessed, and when it has a favourable risk-direct benefit ratio, the trial *is* in the participant's clinical interests anyway. Her ignorance of or misconception about the ratio does not change the fact that her clinical interests are protected. Sreenivasan concludes that such trials have a 'good claim to being ethical'<sup>16</sup> despite the prevalence of the therapeutic misconception.

### ANALYSING SREENIVASAN'S ARGUMENT

By restricting his argument to trials with a favourable risk-direct benefit ratio, Sreenivasan excludes the kinds of clinical trials that most research ethicists find troubling in the face of known misconception. When the research offers net benefits, a potential participant's confusion about the trial's true risk-benefit ratio is not especially worrying. However, when the research poses net risks, a potential participant's ignorance of the ways in which research participation is riskier than standard care might give us cause for concern.

That said, Sreenivasan does appear to identify a set of trials where a patient participant's therapeutic misconception or ignorance of the study's true risk-benefit profile neither invalidates her proffered consent nor requires that the socially valuable research she has agreed to take part in be terminated. If that set is full of socially valuable research, his argument yields a modest result: some clinical trials are not—or should not be—jeopardised by the prevalence of the therapeutic misconception. However, in what follows, I argue that very few trials have this favourable risk-direct benefit ratio, and those that do, preclude the possibility of the therapeutic misconception. Sreenivasan, therefore, fails to identify *any* socially valuable clinical trials that

are ethical when enrolled participants suffer from such a misconception.

### Very few trials have favourable risk-direct benefit ratio

Sreenivasan's argument is plausible only insofar as it is restricted to trials with a favourable risk-direct benefit ratio. The result is only important insofar as there are many trials for which there is a favourable risk-direct benefit ratio. However, this ratio applies to very few trials. This ratio excludes all Phase 0 and I research, and most Phase II, III and IV research, even though this research is carried out only after evidence of effectiveness has been obtained and may directly benefit participants.

Consider a plausible candidate for a trial in which the relation between risks and potential benefits is directly favourable to participants: a randomised controlled trial (RCT) designed to compare the efficacy of two medically indicated treatments. Suppose that this RCT satisfies clinical equipoise since sincere disagreement exists among physicians about the preferred treatment, and so, neither treatment is known to be inferior. This trial might therefore appear to have a favourable risk-direct benefit ratio: after all, just as in clinical practice, patients who have the condition and visit a physician may be prescribed either medically indicated treatment depending upon their physician, so in clinical research, participants who have the condition and are enrolled in this trial may be prescribed either medically indicated treatment depending upon their randomised assignment. In this instance, clinical care and clinical research appear to be directly analogous, which provides *prima facie* reason to think that this RCT is neither riskier nor offers the prospect of less direct benefit than standard care.

But appearances are deceiving. Clinical research requires the collection of data via procedures that are not clinically indicated, including blood draws, scans, biopsies, lumbar punctures and so forth. These are necessary in order to collect the data required to answer the scientific question. But these additional procedures pose risks to participants without offering direct benefits. So while Phase III and IV equipoise-satisfying treatment trials might appear to be rather innocuous—thereby qualifying as favourable risk-direct benefit—this is rarely the case because such trials almost always pose more risk to participants than standard care while offering the same prospect for direct benefit. Thus, even trials that seem like excellent candidates for the favourable risk-direct benefit ratio that Sreenivasan thinks will justify research without adequate understanding of what is disclosed do not actually have that risk-benefit ratio.

### A favourable risk-direct benefit ratio precludes the therapeutic misconception

Even though these trials do not have a favourable risk-direct benefit ratio, Sreenivasan identifies some that do. The problem is that the trials identified are net benefit trials, and they preclude the possibility of the therapeutic misconception.

A favourable risk-direct benefit ratio will only properly apply to research that is directly beneficial and yet does not require additional procedures—for example, quality improvement initiatives or studies of clinical practice that need no more than clinical outcomes to answer the scientific question. These studies are on the cusp of what qualifies as clinical research, and they are a minority of clinical trials. Moreover, since in these trials participants are correct to believe that they are receiving care that is directed at their wellbeing, they do not actually suffer from the therapeutic misconception. If the research offers the patient participants net benefits, there are no failures in understanding of the sort that motivated Sreenivasan's argument.

Thus, even the very few trials that have a favourable risk-direct benefit ratio are not—and cannot be—jeopardised by the therapeutic misconception.

In sum, Sreenivasan fails to identify *any* clinical trials that are ethically permissible in the face of the therapeutic misconception. A favourable risk-direct benefit ratio excludes Phase III and IV equipoise-satisfying treatment trials, and it only includes net benefit trials where participants are correct to have a therapeutic conception. He therefore fails to show that the vast swathes of socially valuable research that motivated his argument can be ethically carried out if participants are ignorant of the study's true risk-benefit profile.

### Sreenivasan's argument is predicated on a favourable risk-direct benefit ratio

The arguments thus far might suggest a response: if Sreenivasan's argument fails because it is restricted to trials with a favourable risk-direct benefit ratio, then his argument should be modestly extended to cover all low-risk research.

However, if Sreenivasan's argument were extended in this way, the justification for not requiring adequate comprehension would be lost. What explains why it is permissible to enrol a patient participant who does not understand the trial's true risk-benefit profile in to a favourable risk-direct benefit trial is that her clinical interests are *already* protected. But if the research activity is riskier than standard care (as it is in all cases other than the favourable risk-direct benefit case), her clinical interests are not protected. Moreover, her ignorance of the trial's true risk-benefit ratio means that she is not well placed to protect her interests. As Sreenivasan himself acknowledges, the plausibility of his argument depends upon its restriction to trials with a favourable risk-direct benefit ratio. However, this restriction also explains why his argument fails.

### LESSONS FROM SREENIVASAN'S ARGUMENT

Research ethicists are not mistaken in thinking that Sreenivasan's argument is important. The mistake has been to think that the value of his argument lies in the conclusion that some clinical trials are ethical despite known misconceptions among participants. The value actually lies in its theoretical setup. It is there that Sreenivasan gestures towards a way of avoiding the unpalatable ethical conclusions that seem to follow from the data on the therapeutic misconception.

If the standard view of informed consent is correct, these data imply that many otherwise ethical clinical trials are unethical, and that many trials currently in progress should be stopped. However, Sreenivasan points out that these conclusions follow only if we assume that the purpose of disclosure is the achievement of understanding. But he suspects that this assumption arises from confusion. He claims that the doctrine of informed consent is just composed of two duties: (1) the duty to disclose and (2) the duty to obtain voluntary consent.<sup>16 21</sup> The assumption that everything that ought to be disclosed must also be understood arises from a mistaken tendency to interpret the two separate duties as one unified requirement. What we aim to do, when discharging the duty to disclose, is to deliver information with the hope that that information will be understood. But it hardly follows from that aspiration that actual comprehension is a requirement of disclosure. If he is right to think that the standard view's substantial understanding requirement arises from confusing an ethical aspiration with an ethical requirement, participants might not need to understand very much at all to give valid consent to research participation. This observation alone allows us to identify three important, but neglected research

questions on informed consent to medical research participation.

### What is the relationship between the requirements for valid informed consent?

Consider this question with reference to the informational requirements for valid informed consent: disclosure and understanding. A recent argument from Tom Walker suggests that Sreenivasan is right that the purpose of disclosure is not the achievement of understanding.<sup>18</sup> Walker argues that information serves different purposes in the informed consent process. Some information is required in order to successfully consent to the activity in question. But other information is required in order to make an informed decision about whether to give or refuse consent. Walker's argument implies that what needs to be understood in order to give valid consent is less than what ought to be disclosed to ensure that potential participants have an opportunity to make an intelligent decision about whether to consent or not.

This is a promising development, but more conceptual research is required on the informational requirements for informed consent. After all, it is widely agreed that disclosure and understanding are necessary conditions of valid informed consent. But if Walker is correct that the profferer of consent can understand enough to give valid consent without understanding everything required to make an informed decision about whether to give or refuse consent, what explains why failing to disclose more than is necessary for a valid token of consent invalidates consent to medical research participation?

The answer might well lie in the relationship between disclosure and voluntariness. It is widely accepted that prospective participants must voluntarily agree to research participation. Yet the kinds of facts expected to be relevant to a prospective participant's enrolment decision are not publicly known. The disclosure portion of the informed consent process therefore puts researchers in a position of considerable power. By withholding certain facts or disclosing them unclearly, a researcher exercises illegitimate control over a participant's enrolment decision and this control can compromise the voluntariness of consent. But when a researcher discharges her duty to disclose properly, she outlines all the relevant information in an appropriate manner thereby avoiding the pitfalls of obtaining consent fraudulently or dishonestly.

All this suggests that Sreenivasan is right to claim that *an* aim of disclosure is to give prospective participants the *opportunity* to understand information that might be relevant to their enrolment decisions. He is also right that it does not follow from that aim that prospective participants must also understand all the information disclosed. Future research should explore whether or not there is another purpose of disclosure that entails that prospective participants do need to understand everything they are told about the research.<sup>19</sup> Future research on this question would provide researchers and RECs with much needed guidance about whether it is permissible to ever accept a voluntary token of consent after a thorough and clear disclosure if the participant does not understand everything that she was told about the study.

### What is the content of the requirements for valid informed consent?

Consider this question with reference to the understanding requirement. If the purpose of disclosure is not the achievement of understanding, what exactly needs to be understood in order for consent to be valid to research participation? Future research

should help us determine whether participants need to understand a lot about the act being authorised (including its purpose and associated risks and benefits) or very little in order to give valid consent.

In other domains in which consent operates, the understanding requirement is rather minimal. For example, I can sell you my laptop without understanding either what you plan to do with it or the true risk-benefit ratio of the property transfer. When relevant information about the research has been disclosed fully and appropriately, why think that the understanding requirement should be any more substantial in the medical context? In fact, even consent to medical research participation cannot require that prospective participants understand all the information that might be relevant to their enrolment decision. Given the nature of medical research, participants are frequently asked to give consent to procedures for which risks are unknown to all parties to the consent transaction. For example, assuming an honest, null hypothesis, a researcher studying the safety of a novel chemical compound for the treatment of tuberculosis will not know whether the drug has certain risks. Since we think that a participant can agree to participate in this trial, we must also think that it is possible to give consent to an activity when ignorant of some of its associated risks.

Sreenivasan entertains an even more radical idea. He claims that “[i]f reliable independent judgment of a trial’s risk-direct benefit ratio is favourable, an individual’s ignorant decision to participate should not be treated any differently from an ignorant decision not to participate.”<sup>16</sup> Since an ignorant decision not to participate in research is obviously valid, why treat an ignorant decision to participate in research any differently?

Brief reflection on the purpose of consent provides an answer. Consent enables competent adults to permit acts that would otherwise be impermissible. When valid, consent has the moral power to alter the rights and responsibilities of consenting parties.<sup>22</sup> This power is predicated on two plausible assumptions. The first is that we have dominion over our body and our property. This translates in to a basic right to independence. The second assumption, which follows from the first, is that others cannot appropriate our body or our property. The basic right to independence generates a correlative duty not to violate another’s independence. When we exercise this basic right we permit another to act in a way that otherwise would be a rights violation.

This analysis explains the asymmetry between ignorant consent and ignorant refusal. If an individual ignorantly refuses to undergo an intrusive procedure, then she might miss out on some tangible benefit, but she is not wronged because not having an intrusive procedure performed does not violate her rights. However, if she ignorantly consents to such a procedure, then she is wronged if the procedure is performed because bodily intrusion without consent does violate her rights.

While prospective participants may not need to understand everything that ought to be disclosed to them in order to give valid consent to study participation, this analysis of consent implies that their authorisation cannot be ignorant or substantially ignorant. In order to exercise their rights, participants must have *some* understanding of what they are permitting. Without it, it is completely unclear how they have altered the normative situation between themselves and the requestor of consent. Moreover, if the requestor of consent knows that the proffered consent is substantially ignorant, it is difficult to see how she can come to believe that the normative boundaries have been redrawn so as to permit acts that would otherwise be impermissible. Future research should explore what needs to be understood to give valid consent to medical research participation. This would help researchers and

RECs develop comprehension tests that accurately evaluate whether participants have understood enough to exercise their autonomy rights.

### What is the relationship between informed consent and the other requirements for ethical medical research?

Informed consent is just one component of ethical medical research. The all-things-considered analysis of what makes research ethical is often complicated. More research is required on the relationship between informed consent and the other requirements for ethical medical research.

Sreenivasan’s argument suggests a good starting place: the relationship between informed consent and risk. The laudable goal of facilitating socially valuable research has created an interest in developing a less burdensome informed consent process for low-risk research. When low-risk research has been overseen by an REC and complies with the regulations, commentators argue along Sreenivasan’s lines: a comprehensive informed consent process offers participants little extra protection while delaying socially and thus morally valuable research. But a plausible risk-adapted account of informed consent must do more than capture the consequentialist intuition that the informed consent process should be less burdensome. It must also guard against diluting the concept of consent. That is, it must guard against requiring only low-grade consent to low-risk research, while insisting on something more substantial—something that approximates genuine consent—to riskier research. Future research on this issue will help guide researchers and RECs in appropriately adapting the informed consent process to the risk level of the research.

### CONCLUSION

In sum, the value of Sreenivasan’s argument does not lie in its practical payoff, but in its theoretical set up. Despite not identifying any clinical trials that are ethical if enrolled participants have a known therapeutic misconception, Sreenivasan’s observations about the informational requirements for informed consent prompt important research questions. More research on these questions promises to yield a defensible view of consent, lessen the burden of ambiguity on those attempting to obtain consent to research participation, and facilitate socially valuable research.

**Acknowledgements** For helpful discussions and comments on earlier drafts of this paper, I thank Joseph Millum, David Wendler, Ben Sachs, Elseline Kingma, Kirstin Borgerson, Marika Warren and two anonymous referees for this journal. An earlier draft of this paper was presented at the Clinical Center Department of Bioethics at the US National Institutes of Health. I thank that audience for their feedback.

**Competing interests** None.

**Provenance and peer review** Not commissioned; externally peer reviewed.

### REFERENCES

- O’Neill O. Some limits of informed consent. *J Med Ethics* 2003;29:4–7.
- Brownword R. The cult of consent: fixation and fallacy. *King’s Law J* 2004;15:223–52.
- Corrigan O, McMillan M, Liddell K, et al. *The limits of consent: a socio-ethical approach to human subject research in medicine*. Oxford: Oxford University Press, 2009.
- Emanuel EJ, Wendler D, Grady C. What makes clinical research ethical? *JAMA* 2000;20:2701–11.
- Appelbaum PS, Roth LH, Lidz CW, et al. False hopes and best data: consent to research and the therapeutic misconception. *Hastings Cent Rep* 1987;17:20–4.
- Flory JH, Wendler D, Emanuel EJ. Empirical issues in informed consent for research. In: Emanuel EJ, Grady C, Crouch RA, Miller FG, Wendler D, eds. *The Oxford textbook of clinical research ethics*. New York, NY: Oxford University Press, 2008:645–60.
- Mandava A, Pace C, Campbell B, et al. The quality of informed consent: mapping the landscape. A review of empirical data from developing and developed countries. *J Med Ethics* 2012;38:356–65.

- 8 Faden RR, Beauchamp TL. *A history and theory of informed consent*. New York, NY: Oxford University Press, 1986.
- 9 Levine RJ. *Ethics and regulation of clinical research*. New Haven, CT: Yale University Press, 1988.
- 10 Beauchamp TL, Childress JF. *Principles of biomedical ethics*. New York, NY: Oxford University Press, 2009.
- 11 National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. *The Belmont report*. Washington: US Government Printing Office, 1979.
- 12 The Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO). *The international ethical guidelines for biomedical research involving Human Subjects*. Geneva, 2002 and World Medical Association. *Declaration of Helsinki: ethical principles for medical research involving human subjects*. Seoul: October 2008.
- 13 Human subjects research protections: enhancing protections for research subjects and reducing burden, delay, and ambiguity for investigators. 76 Fed. Reg. 143 (proposed 26 July 2011).
- 14 Kim S, Ubel P, De Vries R. Pruning the regulatory tree. *Nature* 2009;457:534–5.
- 15 Henderson GE. Is informed consent broken? *Am J Med Sci* 2011;342:267–72.
- 16 Sreenivasan G. Does informed consent to research require comprehension? *Lancet* 2003;362:2016–18.
- 17 Miller FM, Wertheimer A. The fair transaction model of informed consent: an alternative to autonomous authorization. *Kennedy Inst Ethics J* 2011;21:201–18.
- 18 Walker T. Informed consent and the requirement to ensure understanding. *J Appl Philos* 2011;29:50–62.
- 19 Bromwich D, Millum J. Disclosure and consent to medical research participation. *J Moral Philos*. Published Online First: Jul 2013. doi:10.1163/17455243-4681027
- 20 Sreenivasan G. Informed consent and the therapeutic misconception: clarifying the challenge. *J Clin Ethics* 2005;16:369–71.
- 21 Berg JW, Appelbaum PS, Lidz CW, et al. *Informed consent: legal theory and clinical practice*. Fair Lawn, NJ: Oxford University Press, 2001.
- 22 Ripstein A. *Force and freedom: Kant's legal and political philosophy*. Cambridge, MA: Harvard University Press, 2009.



## Understanding, interests and informed consent: a reply to Sreenivasan

Danielle Bromwich

*J Med Ethics* published online April 24, 2014

---

Updated information and services can be found at:

<http://jme.bmj.com/content/early/2014/04/23/medethics-2013-101499>

---

*These include:*

### References

This article cites 11 articles, 2 of which you can access for free at:  
<http://jme.bmj.com/content/early/2014/04/23/medethics-2013-101499#BIBL>

### Email alerting service

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

---

### Topic Collections

Articles on similar topics can be found in the following collections

[Informed consent](#) (239)  
[Legal and forensic medicine](#) (371)

---

### Notes

---

To request permissions go to:

<http://group.bmj.com/group/rights-licensing/permissions>

To order reprints go to:

<http://journals.bmj.com/cgi/reprintform>

To subscribe to BMJ go to:

<http://group.bmj.com/subscribe/>