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The Social Value Misconception in Clinical Research

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ABSTRACT: Clinical researchers should help respect the autonomy and promote the well-being of prospective study participants by helping them make voluntary, informed decisions about enrollment. However, participants often exhibit poor understanding of important information about clinical research. Bioethicists have given special attention to "misconceptions" about clinical research that can compromise participants' decision-making, most notably the "therapeutic misconception." These misconceptions typically involve false beliefs about a study's purpose, or risks or potential benefits for participants. In this article, we describe a misconception involving false beliefs about a study's potential benefits for non-participants, or its expected social value. This social value misconception can compromise altruistically motivated participants' decision-making, potentially threatening their autonomy and well-being. We show how the social value misconception raises ethical concerns for inherently low-value research, hyped research, and even ordinary research, and advocate for empirical and normative work to help understand and counteract this misconception's potential negative impacts on participants.

There is widespread agreement that researchers should help prospective participants make voluntary, informed decisions about enrolling in clinical research. Helping participants make informed decisions both respects their autonomy and promotes their well-being, since participants typically can use information about a study to decide whether enrolling is in their best interest (Dickert, et al. 2017). However, extensive empirical evidence shows that participants exhibit variable and often poor understanding of important information relevant to enrollment decisions, such as the likelihood that they will benefit or suffer harm from participating in research (Mandava, et al. 2012; Afolabi, et al. 2014; Tam, et al. 2015). Bioethicists have given special attention to particular types of misunderstanding or "misconceptions" about research, most notably the "therapeutic misconception" (Appelbaum, Roth, and Lidz 1982), where participants fail to understand some important differences between clinical research and ordinary clinical care. A key ethical concern about these misconceptions is that they can compromise the quality of participants' decision-making, potentially undermining their autonomy or impairing their well-being.

In this article, we describe a previously unidentified type of participant misconception about clinical research: the social value misconception (SVM). While previously identified participant misconceptions primarily involve false beliefs related to risks and potential benefits of clinical research *for study participants*, SVM involves false beliefs related to potential benefits of clinical research *for other people*. We review the literature on participant misconceptions to suggest that SVM is similar to previously identified participant misconceptions in clinical research. We then describe three scenarios in which SVM could occur and threaten participants' autonomy and well-being when making decisions about enrollment: inherently low-value clinical research, hyped clinical research, and some ordinary clinical research. We then suggest how bioethicists

might pursue additional evidence collection and normative analysis about SVM, and discuss possible strategies for mitigating ethically concerning instances of SVM. Finally, we consider and respond to potential objections. Overall, our argument supports ethical concern about SVM sufficient to warrant further empirical and normative research on this newly identified participant misconception.

A few notes before proceeding: First, our discussion concerns only clinical research, although SVM might occur in other types of research involving human participants. We define clinical research as scientific investigation involving human participants that aims to generate knowledge which can be used to protect and promote human health (Tunis, Korn, and Ommaya 2002, 101). Second, for simplicity's sake, we use the term "participants" to indicate *prospective* participants, or people considering study enrollment. Third, we discuss SVM's relevance for participants' enrollment decisions, although SVM also has relevance for decisions to continue participating in research. Fourth, we focus on the beliefs of study participants, although other stakeholders (e.g., investigators, Institutional Review Board (IRB) members, funders) might harbor similar false beliefs about clinical research, which would raise ethical concerns (Henderson, et al. 2007, 1737). Fifth, we focus on false beliefs about the expected social value of particular research *studies*, rather than the value of research programs or clinical research as a whole, since our primary concern lies with participants' decision-making about study enrollment. As we note later, however, general beliefs about clinical research can affect participants' decisions about enrolling in individual studies. Finally, we focus on participants whose false beliefs about the expected social value of studies lead them to decide to enroll. We do not discuss people who refuse to participate because, for example, they substantially underestimate a study's expected social value, although we recognize this also raises ethical concerns (Snowdon, Elbourne, and Garcia 2007).

Participant Misconceptions about Clinical Research

Empirical data show that people who participate in clinical research often misunderstand important facts about that research (Mandava, et al. 2012; Afolabi, et al. 2014; Tam, et al. 2015). Even after going through an informed consent process and participating in a study, many participants predictably form false beliefs about the study's investigational nature and specific purpose, risks and potential benefits of participation, scientific procedures (e.g., randomization), or freedom to withdraw, among other facts. Although these misunderstandings vary by study type, participant demographics, and informed consent procedures, it is likely that common cognitive biases predispose participants to develop such false beliefs (Jansen 2006; Blumenthal-Barby 2016).

We use the term "participant misconception" to refer to a particular type of misunderstanding (or false belief) that participants might have about clinical research. A *participant misconception* is a complex of false beliefs held by a participant in a clinical research study about the study's nature, purpose, or reasonably expected outcomes, whether generally or regarding the participant's own involvement in the study (Horng and Grady 2003; Kimmelman 2007, 40). To illustrate, consider two recently enrolled participants in a phase-I trial of an investigational headache medication. The first participant believes that the investigator is a pharmacist, when in reality she is a physician certified in pharmacology. The second participant believes that he is now employed by the investigator and will receive a salary for his contributions to the study. Both participants misunderstand facts about the trial, but only the second participant has *misconceived* the trial: his false beliefs concern the very nature of the trial and what he reasonably can expect to result from his participation.

Bioethicists have identified participant misconceptions that can compromise the quality of people's decision-making about study participation and therefore can raise ethical concerns. The most well-known is the *therapeutic misconception*, first described by Paul Appelbaum and

colleagues as a "defective understanding of scientific methodology" among participants in psychiatric research who assumed "that decisions about their care are being made solely with their benefit in mind" (Appelbaum, Roth, and Lidz 1982, 320-21). Appelbaum and colleagues argued that such false beliefs about a study's purpose can impair a person's "ability to engage in an accurate assessment of benefits and risks" of participation, thereby undermining the quality of their decision-making or even the validity of their informed consent (320). This raises ethical concerns primarily because such false beliefs about purpose can lead participants to misunderstand a study's reasonably likely outcomes, such as health benefits they will receive from enrolling. Evidence suggests that these beliefs are common in clinical research and can be difficult to prevent or correct (Joffe, et al. 2001; Appelbaum, Lidz, and Grisso 2004; Henderson, et al. 2006; Appelbaum, et al. 2012).

Bioethicists also have identified a *preventive misconception* among participants in clinical research. The preventive misconception occurs when participants substantially "overestimate [the] probability or level of personal protection that is afforded by being enrolled in a trial of a preventive intervention" (Simon, et al. 2007, 371). Like the therapeutic misconception, the preventive misconception can lead research participants to overestimate the expected health benefits of enrollment and thereby compromise the quality of their decision-making. Studies have found evidence of the preventive misconception in trials of vaccines for shingles and HIV (Simon, et al. 2007; Chakrapani, et al. 2013; Ott, et al. 2013).

Bioethicists continue to debate the definition (Horng and Grady 2003; Henderson, et al. 2007; Kimmelman 2007), prevalence (Sulmasy, et al. 2010; Kim, et al. 2016) and ethical significance (Wendler 2012; Miller and Joffe 2013) of the therapeutic and preventive misconceptions. For the purposes of this discussion, however, we remain neutral in these debates. We claim only that participants' misconceptions or false beliefs about the nature, purpose, or

reasonably expected outcomes of clinical research can compromise the quality of their decision-making about study enrollment, thereby potentially undermining their autonomy or impairing their well-being.

On this definition of participant misconceptions, the fact that a person misconceives a clinical research study does not entail that enrollment would be irrational or ethically concerning. This is because not all facts about the study's nature, purpose, or reasonably expected outcomes will matter for a person's decision to participate. Consider a participant who enrolls in a study solely to receive monetary compensation and free health care. However, she believes that the study tests an investigational drug with a novel chemical formulation and mode of delivery, when in fact it tests a "me-too" drug that mimics an approved medication (Gyawali and Prasad 2017). Because the drug's novelty is irrelevant to the participant's motivations for enrolling, her misconception about the study does not compromise the quality of her decision-making about enrollment.

The Social Value Misconception

The late Alan Wertheimer, a prominent philosopher-bioethicist, describes how he suffered from a misconception about clinical research that is different from those discussed above. Shortly after Wertheimer received a leukemia diagnosis, his oncologist encouraged him to enroll in a trial aimed at determining the best time to initiate first-line therapy for his type of cancer (Wertheimer 2014, 127). Wertheimer reports enrolling in the trial for several reasons, including a desire "to contribute to the research so that others might benefit from the study." Unfortunately, his desire went unfulfilled: the trial ultimately terminated because it failed to enroll enough participants to yield meaningful results (Alliance for Clinical Trials in Oncology 2020).

Wertheimer argues that he suffered from a "misconception" about the risk of trial non-completion (2014, 128). He says that when deciding whether to enroll, he did not consider the risk

of non-completion, incorrectly assuming the trial was very likely to enroll enough participants. However, trial non-completion is relatively common, especially in early-phase cancer trials (Cheng, Dietrich, and Dilts 2011; Damen, et al. 2012; Carlisle, et al. 2015). Wertheimer states that he might not have enrolled if researchers had informed him about the risk of non-completion, since he enrolled partly because he wanted the trial's results to benefit other people. He argues that, because people should receive "whatever information can reasonably be expected to be relevant to an intelligent decision about participation" (2014, 128), researchers have a positive obligation to disclose substantial risks of study non-completion from inadequate enrollment.

We propose that what Wertheimer calls the "completion misconception" represents a token of a broader type of participant misconception about the reasonably expected outcomes of clinical research for other people, or its expected *social value*. Clinical research has social value when it produces data that are useful for protecting or promoting the health of current or future members of society (Rid 2020, 294). The social value of research might include other goods, such as non-health benefits for people or benefits for nonhuman animals, but we do not consider these here. We propose that participants in clinical research suffer from the *social value misconception* (SVM) when they have a complex of false beliefs about the expected social value of the research. Misconceiving the extent to which the information generated by a research study can help protect or promote human health can undermine the quality of a person's decisions about research participation. Wertheimer suffered from SVM: his false beliefs about the risks of non-completion led him to overestimate the trial's expected social value. However, if the trial had completed enrollment but other factors unknown to Wertheimer substantially reduced its expected social value (e.g., if the best time to initiate first-line therapy for his cancer was already known when the trial began), he still would have suffered from SVM, which would have undermined his ability to make a decision about enrollment that aligned with his values and preferences.

Indeed, SVM can involve misunderstandings about any number of factors that can contribute to or detract from a study's expected social value. To see this, it is helpful to distinguish two types of consideration in judging the expected social value of clinical research studies: (1) *magnitude of benefit*, or how much the resulting data could improve the health of current or future people, and (2) *likelihood of benefit*, or the probability that the resulting data will lead to improved health (Rid and Roestenberg 2020, 754).

Considerations regarding the magnitude of benefit include the harmfulness of the condition being studied, the potential impact of research results on that condition, and the number of people who could benefit from the research, among other factors. For example, a participant in a trial of a novel statin might misunderstand the trial's expected magnitude of benefit by substantially overestimating the drug's lipid-lowering effects (Lytsy and Westerling 2007). The distribution of health benefits among different groups also can affect the magnitude of a study's value: other factors being equal, research results that improve the health of more disadvantaged people will yield greater social value than results that improve the health of more advantaged people. Distribution of health benefits from results of clinical research that mitigates unjust health disparities can have ethical significance apart from considerations of magnitude of social value, and this might be meaningful to study participants.

Considerations of likelihood of benefit include the quality, feasibility, and rigor of the study's design and execution, the quality of the data analysis and dissemination of the results, the utility of the results for future research and clinical practice, and other factors. For instance, another participant in the statin trial might have realistic beliefs about the drug's potential benefits, but falsely believe the trial will collect enough follow-up data from participants to provide clinically meaningful results (Heneghan, Goldacre, and Mahtani 2017). The inherent uncertainty and incremental nature of clinical research can make it difficult to estimate expected social value with

precision; for instance, it is often difficult to predict a single study's impact on a given health condition. Although this can raise challenges for determining whether participants suffer from SVM, other considerations relevant to expected social value, such as scientific validity and relevance to medical or public health practices, are easier to ascertain.

If previously identified participant misconceptions raise ethical concerns about compromising the quality of participants' decision-making about enrollment, and perhaps even undermining the validity of their informed consent, then so does SVM. Specifically, SVM raises ethical concerns when participants enroll in research for altruistic reasons but misunderstand a study's expected social value. False beliefs about expected social value can impair an altruistically motivated person's ability to balance relevant considerations about their own well-being and the well-being of future patients or society as a whole, thereby impairing their ability to make enrollment decisions that align with their values and preferences. Such a person not only suffers from impaired autonomous functioning, but also might bear burdens and risks of harm that they otherwise would have chosen to avoid, raising ethical concerns about their well-being. If we should have ethical concerns about the autonomy and well-being of research participants who suffer from the therapeutic or preventive misconceptions, then we should have similar concerns for altruistically motivated participants who suffer from SVM.

Importantly, SVM can raise these ethical concerns even when participants have only partially or secondarily altruistic motivations for enrolling in clinical research. For example, if a person wants to enroll in the statin trial primarily to receive financial compensation and secondarily to help others, she might prefer to enroll in an alternative trial that offers similar compensation but has greater expected social value. Or if there is no alternative trial and the statin trial has limited social value, the person might choose not to enroll, just as many people refuse higher-paying jobs that do not make valuable contributions to society (Dur and van Lent 2019). Admittedly, SVM

does not raise ethical concerns about enrollment of participants motivated *exclusively* by the potential direct clinical benefits of a trial or the financial compensation offered. However, many participants cite altruism, such as a desire to advance science or help future patients, as an important motivation for enrollment (Wendler, et al. 2008; Truong, et al. 2011; Jenkins, et al. 2013; Anderson, Borfitz, and Getz 2018; CISCRP 2019; Dubé, et al. 2020a; Baffoe-Bonnie 2022). Even healthy participants who enroll in research primarily for financial compensation may have partially altruistic motivations (Stunkel and Grady 2011; Fisher, et al. 2018).

Three Scenarios of Potential Ethical Concern

In this section, we identify three scenarios in which it is likely that some study participants suffer from SVM in a way that raises ethical concerns similar to those raised by the therapeutic and preventive misconceptions. These scenarios describe features of individual studies or the research enterprise and participants' beliefs about clinical research. While no systematic empirical studies have characterized study participants' beliefs about the expected social value of research, anecdotal reports confirm that some altruistically motivated participants substantially overestimate the extent to which information generated by a study will improve the health of others (Wertheimer 2014; Menchik 2022). We provide reasons to believe this phenomenon occurs in a range of cases.

We assume that participants generally do not receive detailed information about the expected social value of individual research studies. Again, while no systematic data on this issue exist (e.g., a review of informed consent forms for different studies), prominent consent form templates recommend disclosing only general (and generally positive) information about a study's scientific purpose and potential benefits for others (NIH 2023; WHO 2023). We also stipulate that the most ethically concerning cases of SVM involve altruistically motivated participants who substantially overestimate the expected social value of clinical research studies that pose

meaningful risks to them without offering compensating potential health benefits. In these situations, participants' altruistic motivations could be strong enough to lead them to accept substantial research-related risks and burdens based on their false beliefs about a study's expected social value.

Inherently Low-Value Clinical Research

Ethically concerning instances of SVM can occur in *inherently low-value* clinical research studies, which have little or no expected social value due to their objectives, design, implementation, or other aspects. Without disclosure that a study is unlikely to make a positive contribution to human health, people who participate in such research primarily for altruistic reasons likely suffer from SVM; had they known about the study's low expected social value, they likely would have refrained from enrolling. SVM in inherently low-value clinical research raises ethical concerns because it impairs participants' ability to make decisions that align with their values and preferences or to protect their own well-being. Bioethicists previously have criticized research studies that are unlikely to generate valuable results for wasting scarce resources, exposing participants to unnecessary burdens and risks, deceiving or defrauding participants, and potentially damaging public trust (Rid 2020); the possibility of SVM adds a new and distinctive ethical concern about low-value research.

"Seeding trials" conducted by pharmaceutical companies for marketing purposes are an example of inherently low-value clinical research that lacks socially valuable objectives (Hill, et al. 2008; Krumholz, Egilman, and Ross 2011; London, Kimmelman, and Carlisle 2012). For instance, Merck's ADVANTAGE trial randomized participants to nonsteroidal anti-inflammatory drugs rofecoxib or naproxen, ostensibly to improve knowledge about rofecoxib's gastrointestinal side-effects, but marketing executives designed the study primarily "to provide product trial among

a key physician group to accelerate [rofecoxib] uptake" (Hill, et al. 2008, 253). Merck's head of research described the trial as "intellectually redundant," since the company initiated a more efficient, rigorous trial to assess rofecoxib's gastrointestinal safety shortly after ADVANTAGE began (254-256). Since participants could not know the hidden primary purpose of the ADVANTAGE trial or other seeding trials, any altruistically motivated participants likely would suffer from SVM.

Studies that have worthwhile objectives but lack substantial expected social value due to serious shortcomings in their design or implementation represent another type of inherently low-value research. Experts estimate that large portions (as much as 85%) of the hundreds of billions of dollars spent annually on biomedical research and development amount to "avoidable waste" by funding practically irrelevant, methodologically flawed, or inadequately reported studies (Chalmers and Glasziou 2009; Macleod, et al. 2014; Ioannidis, et al. 2014; Glasziou and Chalmers 2018). These problems also afflict clinical research, despite its more explicitly practical orientation than some other types of biomedical research (Yordanov, et al. 2015; Prasad and Berger 2015; Ioannidis 2016): some clinical research studies lack adequate statistical power (Abdullah, et al. 2015; Carlisle, et al. 2015; Bahnam, et al. 2023), utilize unvalidated or irrelevant outcomes (Ferreira-González, et al. 2007; Heneghan, Goldacre, and Mahtani 2017; Haslam, et al. 2019), or generate mostly redundant evidence (Clarke, Brice, and Chalmers 2014; Zarin, Goodman, and Kimmelman 2019).

Many clinical research studies responding to the coronavirus disease 2019 (COVID-19) pandemic had worthwhile objectives but low expected social value due to avoidable design and implementation problems. Some trials of COVID-19 therapeutics suffered from methodological defects like lack of control arms, randomization, or blinding procedures (Bugin and Woodcock 2021; Glasziou, Sanders, and Hoffmann 2020; Hill, Mirchandani, and Pilkington 2022). Many of

the thousands of trials initiated early in the pandemic enrolled too few participants to measure treatment effects accurately, and inconsistency among trials in dosing and outcomes limited the clinical utility of data they generated (Park, et al. 2021). Dozens of underpowered trials of interventions like hydroxychloroquine (Yogendrakumar, et al. 2022) and ivermectin (Hill, Mirchandani, and Pilkington 2022) produced only redundant or clinically irrelevant data (Glasziou, Sanders, and Hoffmann 2020). In these examples of inherently low-value COVID-19 research, any altruistically motivated participants who enrolled without receiving detailed information about a study's limited expected social value likely suffered from SVM, potentially undermining respect for their autonomy and threatening their well-being.

Hyped Clinical Research

Ethically concerning instances of SVM can occur when clinical research is hyped. *Hype* refers to public exaggeration about the potential benefits of research that can lead stakeholders to form unjustified beliefs about its expected social value (Caulfield and Condit 2012; Intemann 2020). Hyped clinical research might be well designed and have substantial expected social value, but various stakeholders exaggerate the likelihood or magnitude of any resulting health benefits. Hype about an area of clinical research can contribute to SVM by inflating participants' expectations about the social value of particular studies, especially when participants do not receive detailed information that allows them to assess reasonably a study's expected value. Hype or excessively rosy projections about the fruits of research might be especially influential when combined with a lack of detailed knowledge of the challenges and complexities of clinical research.

Scholars have identified hype in public communication about the social value of multiple areas of focus in health research, including in genetics and genomics (Caulfield 2018), oncology (Abola and Prasad 2016), regenerative medicine (Kamenova and Caulfield 2015), and

neuropsychiatry (Lilienfeld, et al. 2018). Funders, corporate leaders, clinicians, patient advocates, journalists, and others often unintentionally contribute to hype when attempting to communicate complex scientific information to a wider audience (Caulfield and Condit 2012). Even researchers can inadvertently hype their own studies, partly because they tend to overestimate the likely success and impact of their work (Gan, et al. 2012; Kimmelman, Mandel, and Benjamin 2023). A highly competitive research environment also incentivizes sponsors and investigators to overstate the social value of the research they fund or conduct (Caulfield and Condit 2012; Nuffield Council on Bioethics 2014).[1]

Controlled human infection (CHI) studies for COVID-19 illustrate how hype can lead to ethically concerning instances of SVM. In CHI studies, researchers deliberately infect healthy participants in order to learn about disease mechanisms or gather preliminary safety and efficacy data about investigational vaccines or treatments. Early in the pandemic, prominent scientists and bioethicists argued that COVID-19 CHI studies would accelerate vaccine development, resulting in "savings in human lives [...] in the thousands or conceivably millions;" since "every week that vaccine rollout is delayed will be accompanied by many thousands of deaths globally," the potential benefits justified the acknowledged risks of these studies (Eyal, Lipsitch, and Smith 2020, 1753, 1755; see also Plotkin and Caplan 2020, Chappell and Singer 2020). Enthusiasm for COVID-19 CHI studies spread quickly. Tens of thousands of people registered their willingness to participate through the organization 1Day Sooner (Cohen 2020a; Turk 2020), which advocated for COVID-19 CHI studies with the slogan that "developing a vaccine one day sooner could avert tens of thousands of deaths" (1Day Sooner 2020). COVID-19 CHI study advocates received substantial

[1] It is possible that researchers intentionally or unintentionally hype the expected social value of their studies when communicating directly with participants, which likely would exacerbate SVM. However, we do not have evidence that this has occurred, and our argument does not require that it has.

media coverage (Morrison 2020; Eyal 2020; Singer and Martinez 2020), spurring more advocacy from scientists (Grover 2020a) and politicians (Cohen 2020b), as well as increased public interest in participation (Ramgopal 2020; Kuznia 2020; Grover 2020b).

Despite the enthusiasm for COVID-19 CHI studies early in the pandemic, many expressed significant doubts about the expected social value of such research (Branswell 2020). Experts argued that CHI studies likely could not accelerate vaccine approval: developing a COVID-19 CHI model would require at least 6-12 months, data from CHI studies would be insufficient to demonstrate vaccine safety and efficacy, and high virus circulation made large and more informative vaccine trials feasible (Dawson, Earl, and Livezey 2020; Deming, et al. 2020; Kahn, et al. 2020; Shah, et al. 2020). Indeed, these doubts ultimately proved correct, as researchers developed the first COVID-19 CHI model only after large clinical trials had proven the safety and effectiveness of several vaccines (Rosenheck 2022). The stark contrast between the widespread enthusiasm about the expected social value of COVID-19 CHI studies early in the pandemic and more conservative (and ultimately more accurate) assessments suggests considerable hype about such studies.[2]

Views of potential and actual participants suggest that hype about COVID-19 CHI studies early in the pandemic might have led to ethically concerning instances of SVM. A survey of 1,911 people registered as potential COVID-19 CHI study participants found that 95.9% "wanted to help others and potentially save lives," 79.2% "wanted to contribute to the progress of medicine," and 46.6% "[felt] helpless and [viewed CHI study participation as] a way to do something positive" (Marsh, et al. 2022), although it is unclear how many of these altruistically motivated potential

[2] We do not claim that advocates intentionally fostered hype about COVID-19 CHI studies or that they bear personal responsibility for such hype. Hype often occurs when research stakeholders make honest and well-intentioned attempts to communicate complex science to the public. Several advocates for such studies, including 1Day Sooner, moderated their claims about expected social value as the pandemic developed.

participants substantially overestimated the expected social value of COVID-19 CHI studies. One participant in the world's first COVID-19 CHI study explained he enrolled because of "the potentially massive scientific and social benefits," but acknowledged the "study was not as effective as it could have been," apparently referencing hyped claims about the potential of such research to save thousands or millions of lives (Fraser-Urquhart 2021). We do not know whether participants in the first CHI study (Killingley, et al al. 2022) suffered from SVM, but the evidence suggests that the general hype about the expected social value of COVID-19 CHI studies affected potential participants' beliefs, thereby adding to the risk of ethically concerning SVM in this population. Although hype about these studies was exceptional, hype regularly occurs in other areas of clinical research and can cause SVM in other studies.

Ordinary Clinical Research

Ethically concerning instances of SVM can occur in clinical research that has substantive expected social value which has not been exaggerated in public communication. SVM can occur in this context when participants receive limited information about the studies they are considering for enrollment and lack awareness about different factors that can reduce the expected social value of even high-quality clinical research. In particular, there is reason to believe that altruistically motivated participants can overestimate substantially the expected social value of ordinary studies due to limited knowledge about the nature and organization of clinical research.

In the U.S. and around the world, much of the public lacks understanding of key aspects of scientific research. Globally, 57% of people report knowing "not much" or "nothing at all" about science, with that figure climbing as high as 75% in some regions (Wellcome/Gallup 2019, 28). U.S. respondents report higher than average rates of scientific knowledge, however, another poll found that only 50% of U.S. respondents could identify a scientific hypothesis correctly (Pew

Research Center 2020, 44). Despite the public's limited knowledge, large majorities report favorable attitudes about science: 72% of global respondents express high or medium-level trust in scientists (Wellcome/Gallup 2019, 53), and 83% believe science will improve the lives of people in the next generation (91). A more recent international survey found that 33% of respondents who report low scientific knowledge nonetheless express high trust in science (Wellcome/Gallup 2021, 29).

Any altruistically motivated participants who lack such basic knowledge about scientific research likely will not understand how the nature and organization of clinical research constrain the expected social value of individual studies. First, the incremental and essentially uncertain nature of science means that major advances which substantially promote human health are infrequent and difficult to predict. For example, cancer therapeutics research has yielded substantial health improvements over recent decades (Schilsky, Nass, and Le Beau 2020), but HIV vaccine research has had comparatively limited success (Esparza 2013). Only 14% of drugs tested in phase-I studies eventually receive regulatory approval (Wong, Siah, and Lo 2019, 277-278), and on average that approval occurs after nearly a decade of research with human participants (McNamee, Walsh, and Ledley 2017, 7). By contrast, roughly 40% of patients and the general public believe that it takes fewer than 5 years to develop and obtain approval for a new drug (Anderson, Borfitz, and Getz 2018, 4).

Second, multiple organizational problems undermine efforts to optimize the expected social value of clinical research (Macleod, et al. 2014; Bowen and Casadevall 2015). Researchers struggle to maintain productivity under heavy administrative workloads and high levels of competition (Nuffield Council on Bioethics 2014), institutions inefficiently allocate scarce research resources (Nicholson and Ioannidis 2012; Meyer, et al. 2021), and funders often fail to prioritize studies addressing the most important health knowledge gaps and the highest burden diseases

(Chalmers, et al. 2014; Evans, Shim, and Ioannidis 2014; Pierson and Millum 2022), among other issues. It seems highly unlikely that research participants would have much background awareness of these structural challenges to optimizing the expected social value of clinical research.

HIV cure-related research offers a potential example of ethically concerning SVM about ordinary clinical research. In the past decade, researchers have tested various strategies to "cure" HIV, either by eliminating the virus or controlling it sufficiently to allow an infected person to forgo antiretroviral therapy (ART) for a long time (Pitman, et al. 2018). A cure could lead to major health benefits because HIV continues to cause serious health problems in millions of people, even when they have access to ART. Despite meaningful progress made, however, experts do not expect a cure to be developed in the near future due to multiple scientific and practical challenges (Pitman, et al. 2018; Deeks, et al. 2021). Even if a cure were developed soon, it might not be scalable or effective for all viral strains and populations, limiting its potential social value in the near future (Brown and Evans 2017; Thomas, et al. 2020).

Unfortunately, evidence suggests that some altruistically motivated participants in HIV cure-related research might fail to appreciate the serious challenges to developing an effective HIV cure. Participants in HIV cure-related research often express strong altruistic motives for enrollment (Arnold, Evans, and Vergel 2015; Dubé, et al. 2020b; Villa 2023). In a recent survey of 442 people living with HIV and 144 HIV-specialized healthcare providers, 55% of respondents living with HIV reported believing that a cure for HIV is "achievable within the next ten years," while only 19% of providers agreed (Lau, et al. 2020). These results suggest that some participants in HIV cure-related research might have unreasonable expectations about the time it will take to develop an effective cure, thereby potentially overestimating the expected social value of individual studies.

Although the "cure" moniker raises concerns about misleading people about the potential clinical benefits of study participation (Rennie, et al. 2015), little evidence suggests that researchers or the media have systematically exaggerated the expected social value of HIV cure-related research. Rather, the example of HIV cure-related research reveals how ethically concerning SVM might occur despite researchers' efforts to communicate the incremental and essentially uncertain progress of clinical research with substantial expected social value.

Directions for Future Research and Possible Mitigation Strategies

We have argued that SVM can impair altruistically motivated people's decision-making about study participation, and that this can raise ethical concerns in multiple clinical research scenarios. However, we have provided neither systematic evidence about the prevalence of SVM in clinical research nor definitive guidance for addressing the ethical challenges it raises. Bioethicists need to conduct additional empirical and normative research on both the phenomenon of SVM and on effective interventions to mitigate SVM's negative ethical consequences. In this section, we briefly identify some needs for future research and some possible strategies for mitigating ethically concerning SVM in clinical research.

Future research first needs to characterize the prevalence of SVM in different clinical research contexts, especially those where SVM would raise the most serious ethical concerns. For example, exploratory interviews with healthy participants in an early-phase study that imposes substantial risks could elicit information about participants' motivations for enrolling and their beliefs about the study's expected social value. Data from such qualitative research would allow for the development of surveys to measure participants' social value-related beliefs and motivations in different kinds of studies. This work also would help improve currently limited understanding of the apparently complex ways that beliefs and motivations interact in decision-making about

research participation (Olsen, DePalma, and Evans 2020; Fisher, et al. 2018; Dubé, et al. 2020b; Baffoe-Bonnie 2022).

Empirically characterizing SVM also requires gathering evidence to assess the accuracy of participants' beliefs about social value. Except in cases of egregiously false beliefs, assessing accuracy presents challenges, including a lack of validated measures of the expected social value of various types of clinical research (Minelli and Baio 2015; Binik and Hey 2019; Saylor and Joffe 2023), although some non-validated approaches exist (Rid and Roestenberg 2020; Pierson and Millum 2022). Additional study of researchers', funders', IRB members', and other stakeholders' perspectives about the social value of clinical research would be helpful for making these assessments (Morrell, et al. 2023).

In addition to empirical research about the prevalence of SVM in clinical research, relevant normative and conceptual questions need to be answered. Given certain facts about the prevalence of SVM, how important is it to mitigate SVM compared to other ethical priorities? How should researchers think about potential tradeoffs between addressing SVM versus other participant misconceptions? For example, interventions aimed at addressing therapeutic or preventive misconceptions might encourage unrealistic expectations about expected social value, as they emphasize the goal of clinical research as collecting data to benefit future patients (Appelbaum, et al. 2012; Christopher, et al. 2017). What kinds of misunderstanding about expected social value are ethically consistent with enrolling altruistically motivated participants? Is there some threshold of altruistic motivation to participate in research beneath which SVM does not raise ethical concerns? Bioethicists and research stakeholders should work to address these and other normative questions to develop a more complete ethical assessment of SVM in clinical research.

Improved understanding of the prevalence and ethical significance of SVM in clinical research would allow for the development and evaluation of strategies to mitigate the ethical

challenges it raises. These strategies can take a *value*-focused approach by aiming to improve the expected social value of clinical research to better align with altruistically motivated participants' expectations, or they can take a *belief*-focused approach by aiming to change those expectations so that they align more closely with current realities. While these two approaches are not mutually exclusive, they involve different interventions with different desired outcomes, and one might be more appropriate than the other for certain scenarios.

For example, preventing the occurrence of inherently low-value clinical research, like seeding trials or studies that will generate only redundant results, represents one reasonable, value-focused approach to addressing SVM. Disclosure of low expected social value to participants in such research might mitigate SVM, but the superior strategy is for researchers, funders, regulators, and other stakeholders to coordinate to stop inherently low-value studies before they begin.[3] Bioethicists have argued for reasons unrelated to participant decision-making that clinical research must have sufficient expected social value (Wendler and Rid 2017; Wenner 2018), and ethical concerns about SVM in low-value research provide additional support for these arguments. Although we agree with these arguments for promoting the social value of clinical research, our argument does not assume that all clinical research studies ethically must meet some minimum threshold of expected social value. We also note that even skeptics of a social value requirement for clinical research have agreed that studies must meet some minimum threshold of expected social value when they recruit altruistically motivated participants (Wertheimer 2015, 306-307).

Hyped clinical research, in contrast, seems to call for a belief-focused approach of mitigating SVM by correcting participants' inflated expectations even about studies with substantial social value. Researchers might attempt to debunk hype by providing participants with realistic

[3] Except perhaps in egregious cases, it is unclear whether IRBs have the necessary expertise to determine whether proposed studies have sufficient expected social value.

information about expected social value; for example, researchers could have explicitly informed potential participants in COVID-19 CHI studies that such studies were unlikely to save millions of lives in the near future. Alternatively, stakeholders in the clinical research enterprise could work to reduce hype generally by implementing specific reforms, such as improved communications training for scientists and additional research on effective public messaging strategies for scientific organizations (Bubela, et al. 2009). Recent initiatives to improve understanding of clinical research among members of the public have shown encouraging results (Simon, et al. 2019; Getz and Getz 2019), and similar activities could help inform the public about the likelihood that individual research studies will yield valuable results.

Both value-focused and belief-focused strategies might help prevent or mitigate ethically concerning instances of SVM in ordinary clinical research. For example, in HIV cure-related studies, researchers could attempt to counteract participants' overestimation of expected social value by providing relevant information about the expected time and inherent uncertainty involved in developing an effective intervention. In addition, research institutions might implement various proposed reforms to optimize the expected social value of clinical research, such as improved prioritization and portfolio-level assessment (Macleod, et al. 2014; Ioannidis 2016; London and Kimmelman 2019; Binik and Hey 2019; Meyer, et al. 2021; Pierson and Millum 2022; Saylor and Joffe 2023). Improving the efficiency of research is valuable for its own sake, but it could have the added benefit of properly aligning recruitment efforts for clinical research with the beliefs of altruistically motivated study participants, thereby mitigating SVM.

As with the prevalence of SVM itself, bioethicists need empirical evidence to assess the absolute and relative effectiveness of possible mitigation strategies. Although limited data suggest that informed consent documents do not comprehensively address social value (NIH 2023; WHO 2023), we know little about how researchers communicate about social value with study

participants. Such evidence is needed to develop effective belief-focused interventions, which might include providing more helpful information about a study's purpose and expected outcomes in informed consent documents, showing explanatory videos or graphics to prospective participants, or adding questions about expected social value to evaluations of participant understanding (Christopher, et al. 2017; Campbell, et al. 2022). Addressing expected social value in informed consent processes might be insufficient or counterproductive, however, as bioethicists have highlighted various deficiencies in informed consent processes in clinical research (Henderson 2011; Mandava, et al. 2012; Grady 2015; Tam, et al. 2015), and making such processes lengthier and more complicated might exacerbate these problems.

Objections and Responses

We have argued that enrolling altruistically motivated people in clinical research when they suffer from SVM raises ethical concerns similar to those raised by enrolling participants who suffer from therapeutic or preventive misconceptions. One might object to this conclusion by arguing that participant misconceptions raise ethical concerns only when they undermine the validity of informed consent to participate in research (Horng and Grady 2003; Appelbaum, Lidz, and Grisso 2004), and we have not shown that SVM can invalidate consent. Unlike therapeutic or preventive misconceptions, a participant can egregiously misconceive a study's expected social value while fully understanding the risks and potential benefits related to their own body and health, and one could argue that this understanding suffices for valid informed consent.

This objection rests on the unstated premise that only false beliefs relevant to *self*-regarding values and preferences can invalidate informed consent, not false beliefs relevant to *other*-regarding values and preferences. There are two problems with this premise. First, as Wertheimer notes, nobody has offered a principled argument for it (2014, 128). Second, the premise seems

false when applied in non-research contexts: Imagine a person considering donating a kidney to a relative who will die without the organ and who cannot receive one from another source. The medical team ensures that the prospective donor fully understands the risks and potential benefits of kidney donation for the donor's own body and health. However, the medical team fails to inform the prospective donor that the relative has less than a 5% chance of surviving for a year after transplantation, which is much lower than the prospective donor's expectation. Intuitively, it seems that the medical team does not obtain valid informed consent from the donor unless they disclose the relative's unfavorable survival prospects, even though this information concerns the donor's other-regarding values and preferences.[4]

Even assuming that SVM cannot threaten the validity of informed consent, the assumption that participant misconceptions raise ethical concerns only when they pose this threat is implausible. We have shown how SVM can lead to poor decision-making and reduce the likelihood that important decisions about participation in clinical research align with people's values and preferences and are consistent with their well-being. As with the therapeutic and preventive misconceptions, SVM threatens altruistically motivated people's free, informed, and safe participation in clinical research, which is inherently ethically concerning irrespective of narrower concerns about validity of consent.

Another objection holds that if an IRB determines that a clinical research study has a reasonable ratio of risks to potential benefits for participants, then SVM is not ethically concerning, since these false beliefs will not lead participants to take on unreasonable risks. While altruistically motivated participants with false beliefs about a study's expected social value are not necessarily

[4] Some bioethicists argue that providing valid informed consent to participate in clinical research does not require understanding its nature, purpose, risks, or expected benefits (Millum and Bromwich 2021). While we do not have the space to address this ongoing debate, we here claim only that if therapeutic and preventive misconceptions threaten the validity of informed consent to participate in research, then so does SVM.

more vulnerable to harm than other participants, respect for autonomy generally requires allowing participants to make informed decisions about whether to accept any substantial added risk of harm or burdens by enrolling in research. Even when clinical research poses no substantial risks to consenting participants, respect for autonomy supports providing accurate information about expected social value to avoid taking unfair advantage of altruistically motivated people.

A third objection argues that researchers and other stakeholders lack a moral obligation to address SVM because they typically cannot know the precise expected social value of their research, and therefore cannot be obligated to provide such information to study participants. As we noted above, uncertainty is inherent in scientific research, and researchers often cannot accurately predict the short- and long-term impacts of their work (Kimmelman, Mandel, and Benjamin 2023). However, researchers still can disclose helpful information to overenthusiastic participants who otherwise might misconceive a study's expected social value, such as the study's known limitations, internal and external factors that might reduce expected social value, and the inherent uncertainty and incremental nature of science. The clinical research enterprise also can develop and implement tools that would improve predictions and communication about expected social value of research studies and programs (Chalmers, et al. 2014; Minelli and Baio 2015; Ioannidis 2016; Binik and Hey 2019). The previous section highlights the need for additional evidence to design and prioritize effective interventions, but the current evidence gap does not obviate moral obligations to take reasonable measures to address the threat SVM poses to participants' autonomy and well-being.

Finally, one might raise a consequentialist objection that even if SVM is ethically concerning and can be mitigated effectively, informing altruistically motivated participants about the realities of expected social value would undermine recruitment in many studies, ultimately damaging the clinical research enterprise. This result seems most plausible for inherently low-value

clinical research, but in that scenario consequentialist reasoning seems to favor mitigating SVM: not only would it promote good decision-making among altruistically motivated participants, but by impeding general recruitment it would reduce unjustified harm to participants and waste of scarce resources caused by low-value clinical research. For clinical research with substantial expected social value, it is not obvious that providing participants with helpful information about expected social value would lead to drops in study recruitment. After all, many people participate in research for personal health or financial benefits, yet efforts to mitigate other participant misconceptions have not reduced willingness to participate (Christopher, et al. 2017; Campbell, et al. 2022). Even if counteracting SVM by giving participants more information would reduce recruitment enough to impede the conduct of certain types of clinical research, it seems that would be a cost worth bearing to promote participants' autonomous decision-making and to protect their well-being.

Conclusion

Like with previously identified participant misconceptions, misconceptions about the expected social value of clinical research threaten to undermine the quality of decision-making about study enrollment, which can be ethically concerning for altruistically motivated participants. The available evidence suggests that false beliefs about expected social value can influence the decisions of altruistically motivated participants in inherently low-value, hyped, and even ordinary clinical research studies. Bioethicists, clinical researchers, and other stakeholders in the clinical research enterprise should work together to gather more empirical evidence about SVM and to understand its ethical significance. This knowledge will guide the development of effective strategies—such as preventing inherently low-value research, reducing research hype, and

improving general knowledge about clinical research—to reduce the occurrence of SVM and its negative impacts on participants.[5]

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