Human Challenge Trials

PHIL 334: Pandemic Ethics

Contents:

Human Challenge Trials

What are they?

In a human challenge trial, healthy people are intentionally exposed to a disease.

This helps scientists to rapidly discover things... like whether, for example, trial participants who are given a potential vaccine are protected against the disease, when that protection kicks in, and to what extent it works (does the vaccine prevent infection, all symptomatic illness, serious illness and/or death?)

Nir Eyal on Human Challenge Trials

Risk & Research

Research ethics should not just attend to the **risks** of study participation.

It also needs to consider **benefits** from participation.

And then consider the **balance of the two**.

After all, this is what doctors do when prescribing a surgery or potentially toxic treatments...

Risk & Research

"What matters in assessing the offer that researchers make to candidate participants is not simply the so-called absolute risk, better described as the raw or contributing risk, that comes with the challenge—whether viral exposure poses only minor or controllable risks or, alternatively, more serious ones—but **the net risk**: the risk from participating in that trial minus the risk that the same person would face otherwise." - Nir Eyal

Risk & Research

In short, if researchers conducting challenge trials act as recommended, admittedly, the probability of getting infected would remain larger inside a challenge trial than either outside any trial or in a standard efficacy trial; but the probability of death or disability is likely to be much smaller inside a challenge trial than in these alternative scenarios. Overall, $a \times b$ could be smaller for any individual inside the challenge trial than either outside any trial or in a standard efficacy trial. What the individual would lose in the probability of averting infection (with that probability rising) she could gain in better protection from death.

a = probability of getting infected with COVID-19

b = probability of either dying from, or developing a long-term disability as a result of, the infection

$a \times b$ is the probability that matters.

Risk & Research

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Therefore, **it cannot justify paternalistic protection** when adults with the requisite decision-making capacity wish to help researchers do enormous good."

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So, if adults (with the requisite decision-making capacity) want to participate, why stop them?

Risk & Research

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If S consents to something, and is informed about what they are consenting to, then, unless they are subjecting themselves to a very high risk of death or disability, we should let them do it.

Can participants in human challenge trials *really* consent?

Informed Consent

What does *informed consent* mean to you?

Informed Consent

The Duty of Informed Consent is Actually Two Duties – but they both need to be satisfied!

1. a duty to obtain the voluntary agreement of patients or trial participants before treatment or enrolment; and
2. a duty to disclose adequate information to the patient or participant before seeking this agreement.

Informed Consent

Things Get Messy…

What is adequate information?

How can we be sure that consent is voluntary?

Do we need to be sure of the enrollee's *comprehension* of the details for informed consent to be established?

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What is **adequate** information?

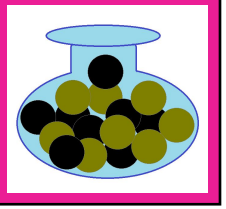
Risk vs Uncertainty

Can enrollees give informed consent when there is much we do not know about COVID-19?

Risk vs Uncertainty
Is there a difference between doing something *risky* and doing something completely *unknown*?

"high **uncertainty** among experts is perfectly compatible with valid *informed consent*: consent can remain valid when researchers' understanding is highly incomplete, or even completely wrong".
- Steel, Buchak, & Eyal

Risk vs Uncertainty



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Consider the following two bets:

(1) I will flip this fair coin. If it lands heads, you win $10. If it lands tails, you lose.

(2) I will draw a marble from this urn (which contains only black and white marbles). If I draw a black marble, you win $10. Otherwise, you lose.

Which would you prefer?

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Is consent given under conditions of **uncertainty** less valid than under conditions of **risk?**

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Not according to Steel, Buchak, & Eyal

Uncertainty

"Can valid informed consent to participation in research be obtained given high levels of uncertainty? SBE answer the question in the positive, and we agree with their answer. They rightly point out, that **by its very nature, research addresses areas where there are gaps in existing knowledge; and that accordingly, if a (near-) complete understanding were required, then valid informed consent for research would seldom be obtainable.** Complete understanding of the options before us and the risks and benefits they involve is not required because **we can be aware of the partiality of our understanding, and take our ignorance into account in our deliberations.**"

Highly Incomplete VS Completely Wrong

Completely Wrong

But can valid consent be given on the basis of error and wrong understanding? SBE claim that it can: 'consent can remain valid when researchers' understanding is highly incomplete, or even completely wrong' (2, our emphasis). Here SBE are mistaken, because they ignore the different effects which error and mere lack of knowledge have on our ability to provide valid informed consent. Incomplete knowledge and understanding differ from wrong understanding in their effect on the validity of consent, because when we suffer from incomplete understanding, we can know that our understanding is incomplete, and take our lack of knowledge and understating into account in our decisions and deliberations. In contrast, when we suffer from a false belief, we cannot take the fact that our belief is false into account in our deliberations. One cannot hold a false belief while knowing that it is false."

Can you consent if you are misinformed?

Consent & COVID

"To determine whether to permit COVID-19 CHI trials, decision-makers must consider what the chances are that consent obtained under current conditions of still emerging understanding be based on error in a way that undermines the validity of consent. This is a question that cannot be answered from the armchair. But one thing is clear: given the limited evidence on which our understanding of COVID-19 is based, chances that participants be provided with misleading descriptions of important features of COVID-19 CHI trials is much greater than the chances that participants be provided with misleading descriptions of trials involving better understood diseases.

Therefore, concerns about the validity of consent to COVID-19 CHI trials are much more serious than concerns about the validity of consent to more standard medical experimentation."

Do we need to be sure of the enrollee's **comprehension**?

Comprehension & Informed Consent

Gopal Sreenivasan argues that comprehension is NOT a necessary condition of valid consent.

Comprehension & Informed Consent

The point of disclosing information to the patient is to impart a certain grasp of the procedure or protocol in question. So, the caregiver should aspire to produce adequate comprehension (that is part of the duty of disclosure). However, success in producing comprehension is not required.

As caregivers, we should want to produce comprehension, but our minimal duty is to strive to do so by providing adequate information in a comprehensible form.

Is it ever okay to deceive a patient? Why or why not?