And there we go again: the ethics of placebo-controlled RCT in case of catastrophic illness

Udo Schuklenk

Reading the exchange between Halpin, Savulescu, Talbot, Turner and Talman reminds one starkly and uncomfortably of the issues AIDS activists faced in the 1980s and 1990s. Some of the trial designs in those days were sufficiently bad that patients could not be recruited in the numbers required to run them, the sacrifices they demanded from patients in terms of their very survival were simply too extreme. Anthony Fauci, at the time director of the US National Institute of Allergy and Infectious Diseases (NIAID), reportedly conceded that “the randomised clinical trial routinely asks physicians to sacrifice the interests of their particular patients for the sake of the study.”

Mainstream bioethicists defended the coercive offers that were extended at the time to patients by the research establishment, pretending that the choice of joining a placebo-controlled trial with an experimental agent or having no chance to access an experimental agent were reasonable options in a reality absent of any gold standard of medical care. John Arras, for instance, argued that “[b]y entering a protocol, subjects enter into a moral relationship with researchers by promising ... to abide by certain restrictions in return for the benefit of participation. Dropping out of an ethically designed study merely because one has to be randomized to placebo, pooling drugs, or taking unapproved remedies all amount to violations of this promise.”

His perception of the reality is markedly different to that of prospective trial participants such as Martin Delaney who wrote, “It is as if I am in a disabled airplane, speeding downward out of control. I see a parachute hanging on the cabin wall, one small moment of hope. I try to strap it on, when a government employee reaches out and tears it off my back, admonishing, ‘You cannot use that! It does not have a Federal Aviation Administration sticker on it. We do not know if it will work’.”

Or take an anonymous contributor to an on-line discussion group who stated bluntly, “I hate to say it but we are no more than lab rats to these people.” Activists and patients questioned whether those trials were ethically designed and indeed denied that the promises made by trial participants were truly voluntarily made.

Like Lee Halpin and Julian Savulescu in this paper I argued at the time that patients suffering from catastrophic illnesses with the potential to kill in a reasonably short period of time should be permitted access to experimental agents. Little has changed since then. Access to investigational new drugs is a bit easier, but the fundamental access issue remains unresolved. Ethicists continue to argue Arras’ case as well as the opposing point of view.

We surely need to develop mechanisms that render the choice to participate in a placebo-controlled RCT a truly autonomous choice. This crucially implies voluntariness. You are not a true volunteer if reasonable alternative avenues to investigational new drugs outside the clinical trial system are closed to you in order to ‘encourage’ you to participate in a placebo-controlled trial. Permitting patients supervised access to investigational new drugs seems to be a reasonable solution to this problem. Incidentally, this would also resolve another problem plaguing trials of this nature, their huge drop-out rates. The late Alvin Novick, at the time a biology professor at Yale University noted in a 1993 article published in the AIDS and Public Policy Journal that “patients dropped out of almost all of the trial presented to us at a rate that appeared to compromise interpretation of the results. Sometimes they fake entry data, do considerable detective work to identify whether they are on a placebo or drug, identify the dosage they received in dose-ranging trials, or otherwise behave actively, by their view of self-interest, rather than as passive subjects.”

I do not know to what extent amyotrophic lateral sclerosis (ALS) patients are as well-organised as AIDS patients were in those days. What is clear to me is that the latter’s aggressive political activism ultimately resulted in unprecedented clinical research aimed at developing life-preserving medications. They succeeded. Other patient groups could do worse than learning the relevant lessons from AIDS activists. Their political pressure changed the way how we go about recruiting patients into clinical trials, too.

One final note: for patients to appreciate the nature of the risk they are taking when they choose to take experimental agents, it would help if we reframed from describing them as ‘drugs’ or ‘medicines’ as the ‘physician’s perspective’ in this paper does. Unless something is approved as a drug or medicine as a result of a properly constituted clinical trial, all it is, is a chemical for which there exists anecdotal evidence that it might work—sometimes possibly less than that. We do not do understandably desperate patients any favours by rhetorically changing the nature of what it is that we really know about these chemicals. For patients to appreciate the magnitude of the risk they are about to take if they access experimental agents is a vital component of enabling them to make an informed choice. This can sometimes require of them to understand that nothing is actually known about the magnitude of the risk they wish to undertake. It is unhelpful to muddy these murky epistemic waters by calling experimental agents ‘drugs’ or ‘medicines’ under such circumstances.

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REFERENCES

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