

Assessment of the Right-To-Try law: the pros and the cons

Short running title

Right-To-Try

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Introduction

On May 30th, 2018, the Right-To-Try bill, allowing the use of experimental, non-Food and Drug Administration (FDA) approved drugs as a last resort for those unable to participate in clinical testing who have also exhausted all other treatment options, was signed into law¹. At the time this bill was signed, 38 states had passed similar Right-To-Try laws; this law is nationwide¹. The requirements for granting approval of experimental drug treatment under Right-To-Try laws are: 1) a terminally ill patient has exhausted all other treatment options and is ineligible to participate in clinical trials, 2) the experimental drug passes FDA Phase 1 clinical testing, 3) the patients' health care provider or treating physician must recommend and approve the experimental treatment, 4) the pharmaceutical manufacturer must approve the drug for use as an experimental treatment, and 5) patients' written informed consent is required^{2,3}. While some experimental drugs may improve some patients' condition(s), adverse health effects or no health improvement are more likely.

In the following text we weigh the pros and cons of the federal Right-To-Try law.

Cons

Limited Patient Understanding

One requirement before beginning experimental drug therapy is patient informed consent. Consent documents are often confusing, written in a way that is difficult to understand, containing highly technical terms at great length, which can result in patients missing or misunderstanding the gist of the experiment^{4,5}. Similarly, there may be misunderstanding of experimental drugs and their likely success rates, as well as the potential of therapeutic misconception⁶. Terminally ill patients who feel like they are running out of time may be swayed by the false hope provided by an experimental procedure, which can outweigh potentially detrimental effects of the experimental drug and other unintended consequences.

Lowered Trust in the FDA

The FDA's clinical trial and review process took over 50 years to establish in order to ensure pharmaceuticals are safe for their intended use⁷. Although this highly regulated process can require up to 15 years for a drug to receive FDA approval, it is an effective method that weeds out most ineffective and/or dangerous drugs⁸. Arguably, Right-To-Try laws are hypocritical because they rely on the FDA process of determining the toxicity and possible side effects of products in Phase 1 testing, but this argument ignores the fact that drugs need to be rigorously tested to be deemed safe for widespread use³. There is a need to protect patients' trust in the clinical research enterprise.

Financial Consequences

Marginalized patients could be vulnerable to exploitation through Right-To-Try. The legislation does not contain incentives for insurance companies to cover experimental treatment costs and the potential outcomes of the treatment^{2,9}. Insurance companies in many states that passed Right-To-Try laws have denied hospice coverage, home health care coverage, and even health care coverage for at least 6 months after treatment^{2,9}. This denial of coverage creates a financial burden left for the families, who often cannot pay.

Decreased Liability

One of the most problematic issues with the federal Right-To-Try legislation is provided immunity from liability for physicians and pharmaceutical companies^{2,4}. Without FDA oversight, pharmaceutical companies can push unsafe drugs on sick patients. While it is presumed that primary care physicians

have their patients' best interest in mind, physicians can own pharmaceutical company stock and charge patient treatment fees². Pharmaceutical companies, for their part, need have no fear that any negative outcomes from experimental drugs will hurt the chances of the drug becoming FDA approved, as this legislation prohibits the FDA from including negative outcomes of experimental treatments in the data that is used to approve the pharmaceuticals^{2,10}. Lack of systematic reporting of adverse events may result in decreased information for the public and providers.

Safety Consequences

Nearly 70% of drugs pass Phase I testing¹¹. However, most drugs that pass Phase I will be deemed unsafe or ineffective, failing to pass subsequent stages¹¹. There is a low probability that experimental drugs tested in early-stage research will significantly benefit patients and a higher probability that side effects from experimental interventions could worsen their condition^{2,12}. Additionally, the FDA expanded access process has been revised to be more transparent and to take less time¹³: patients can now complete the expanded access request form within an hour¹³. Right-To-Try legislation has helped make under tested drugs more readily accessible by reducing FDA oversight, which was created to protect patients and consumers from unsafe pharmaceuticals. Another consideration is the growing epidemic of counterfeit medicine; another reason to protect the integrity and safety of the drug development process¹⁴.

Pros

Experimental drugs may extend life

In most cases, experimental treatments have not yet proven effective. However, they can potentially extend life¹⁵. Compassionate use has been used in epidemics with a high death rate (e.g., the Ebola outbreak in 2013-2016)^{16,17}. Widely untested therapeutic vaccines were given to people living with Ebola in hopes of improving their condition¹⁸. Given a setting of compassionate use, even unsuccessful treatment may help strengthen patients' trust in healthcare systems due to potentially positive health outcomes.

In line with Expanded Access

The case for the terminally ill to try potential life extending drugs has been addressed by the FDA^{8,13}. Dr. Scott Gottlieb, Commissioner of the FDA (May, 2017-present), has stated that the FDA approves almost all expanded access requests: high urgency immediately or over the phone, and all other requests within a few days¹³. The Right-To-Try legislation is very similar to the Expanded Access program in that it recognizes that a streamlined process is necessary if experimental drugs are to reach patients who may not have any other options.

Gives patients more options

Supporters of the Right-To-Try law argue that the law will not replace Expanded Access, but will create another avenue to streamline the process for experimental treatments³. Although the FDA receives around 1000 requests annually for experimental drug therapies, many such therapies never make it to the FDA^{12,13}. Confusing online forms and multiple attachments can be barriers to getting experimental drugs approved for use, and by the point of approval patients' conditions may have worsened significantly. Right-To-Try laws are intended to further streamline this process, allowing patients to work directly with doctors to acquire non-clinically tested drugs, bypassing the FDA and providing multiple options for all terminally ill patients to acquire potentially life extending drugs. The federal Right-To-Try law intends to give people more control over their life/health. Even if experimental treatments are ineffective, the argument is that people should have a choice to at least try a drug that may produce medical benefits. Similarly, medical aid in dying allows patients to make important medical decisions towards the end of their life¹⁰. Some argue that if patients have the right to end their

life with medical aid in dying, they should also have the right to try to extend their lives with experimental drugs¹⁹. Personal choice over what happens to one's health near the end of life is aligned with the ethical principle of autonomy and can be empowering.

Final Thoughts

One of the main principles the Right-To-Try law was built upon was to reduce pain and suffering. However, bypassing FDA regulations means the data that would normally be available for physicians and clinical researchers, such as dosage, drug administration, and side effects, will be limited. The potential for lowered trust in the clinical research enterprise, financial and safety consequences, decreased liability, and limited patient understanding clearly outweigh the potential benefits of the experimental drugs tested outside the FDA purview.

That being said, healthcare systems are often paternalistic and may treat the disease rather than the patient. Academics are similar in how they choose research projects and participants. For patients to make a well-informed decision, they must be provided good, clear knowledge regarding the benefits and limitations of experimental treatments¹⁹. These patients also must have enough information to assess the risks of these treatments, including full comprehension of the severity of possible side effects as well as financial costs. In complicated clinical research, proper explanation and understanding of these issues may take several pages of text, and key points may get lost in the shuffle. However, the autonomy of those at the end of life should be respected, and terminally ill individuals should be given the opportunity make well informed decisions. This is why we side with the patient to have more options via Right-To-Try.

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