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The ethical plausibility of the 'Right To Try' laws

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ABSTRACT

'Right To Try' (RTT) laws originated in the USA to allow terminally ill patients to request access to early stage experimental medical products directly from the producer, removing the oversight and approval of the Food and Drug Administration. These laws have received significant media attention and almost equally unanimous criticism by the bioethics, clinical and scientific communities. They touch indeed on complex issues such as the conflict between individual and public interest, and the public understanding of medical research and its regulation. The increased awareness around RTT laws means that healthcare providers directly involved in the management of patients with life-threatening conditions such as cancer, infective, or neurologic conditions will deal more frequently with patients' requests of access to experimental medical products.

This paper aims to assess the ethical plausibility of the RTT laws, and to suggest some possible ethical tools and considerations to address the main issues they touch.

1. Introduction

The Right to Try (RTT) laws originated in USA in 2014 at the Goldwater Institute, a conservative libertarian public policy think-tank in Phoenix, Arizona (Bernick, 2016). They allow terminally ill patients (patients in an advanced stage of a disease with an unfavorable prognosis and no known cure) to request access to early stage experimental (with as-yet-unknown efficacy and adverse effects) medical products (drugs, treatments, biologics, and other medical devices), directly from the producer, removing the oversight and approval of the Food and Drug Administration (FDA). Although based on the Goldwater Institute's blueprint, they vary between different states. The main RTT laws requirements (Rubin and Matthews, 2016) are:

- The patient has a diagnosis of a terminal disease (which in some states includes permanent coma) and no other treatment options are available.
- The experimental product has passed Phase 1 safety testing and is at least in early Phase 2 safety and efficacy testing.
- The patient's healthcare provider (HCP) recommends the experimental medical product.
- The patient, or a designated guardian, has given informed consent to take this product.

The HCPs are expected to give patients a description of the best and worst possible outcomes using an experimental treatment. However, the RTT laws absolve HCPs and producers (the pharmaceutical or biomedical company or manufacturer developing the product) from legal liability from any harm the experimental medical product can cause to patients. RTT laws are underpinned by the presumption of patients' capacity to weigh the risk and benefits and make informed medical decisions based on the information provided by their HCPs, and on their own values and desired outcomes.

The first RTT law was passed in Colorado in 2014, and currently (November 2017) there are RTT laws in place in 38 states.[1] RTT bills have been introduced by both Republicans and Democrats and they have passed with unanimous support. These laws have proved very popular and have received significant media attention. In contrast, they have also received almost equally unanimous criticism by experts in the bioethics, law, clinical and scientific communities (Rubin, 2015).

1.1. Background: FDA expanded access

Before entering the heart of the controversies, some background information is needed to understand the context in which RTT laws have emerged. When available treatments are ineffective, some patients with serious or terminal illnesses may wish to try experimental medical products, in the hope of receiving therapeutic benefit. The standard

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[1] http://righttotry.org/in-your-state/.

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way to access such experimental products is by participating in a randomised control trial (RCT). As known, new medical products are not available to the public until they have been tested in Phase 3 of clinical trials; shown evidence of safety and efficacy; and gained approval from the FDA. This testing and approval process can take up to 10–15 years. RCTs also require specific eligibility criteria that may preclude certain patients from participation, and these criteria often exclude terminally ill patients because they are more likely to develop adverse outcomes, risking both their lives and to jeopardise the RCT. Currently RCT access is also limited by patient geographical location, with rural areas particularly penalised. Therefore, terminally ill patients who do not qualify for or do not have access to a RCT may die waiting for a medical product to be approved and accessible. Moreover, terminally ill patients who can access RCTs, may not wish to risk to take the 50% chance of being assigned to a control group (who often receives a placebo or an already approved treatment, which would be ineffective for such patients) and therefore not obtain timely access to the experimental medical product they seek.

These are among the main factors that have led some patients to seek experimental medical products on their own, also illegally from black or 'grey' markets (from other patients who sell their pills or share the ones they got in trials) (Leonard, 2009). Since the 1970s, the American patients have also legally pressured the FDA to expand access to experimental medical products. Under current FDA regulations, patients with serious or life-threatening conditions can apply for Expanded Access (EA) to experimental treatments outside of a clinical trial and before the experimental medical product has been approved by the FDA.[2] This requires approval by both the FDA and by an independent Institutional Review Board (IRB) at the hospital or institution where the treatment will be administered. The objective of the EA programme is to balance speed and safety of access for the requesting patient, without interfering with the conduct or completion of the RCT (Food and Drug Administration, 2016). Some important measures help to achieve this objective:

- The IRB acts as an independent third party whose tasks include reviewing research protocols; assessing the risks and benefits to safeguard patients; review consent forms, in particular the language and terminology used, to help ensuring that consent is informed and voluntary.
- Before the FDA considers a request for EA the producer must agree to provide access to the product outside a RCT. The FDA can act as mediator between the patient and the producer, but has no authority to override a producer's decision to not provide access.
- Once access is given, the HCPs have to report follow-up clinical data about the patient to the FDA (Servick, 2014).

EA is normally granted for experimental medical products in Phase 2 or 3 in circumstances where there are no alternative therapies and the patients are ineligible or unable to participate in a RCT. It is important to highlight that EA also allows patients with immediate life-threatening conditions to apply for access to experimental medical products that have passed Phase 1 of RCT (Dresser, 2015) – the same threshold of the RTT laws. However, unlike the RTT laws, the FDA always requires data suggesting the medical product is safe enough to give to patients.

In recent years, the FDA has approved more than 99% of EA requests it received and has speeded up the approval process (Miller et al., 2017). The current FDA EA form normally takes 45 min for HCPs to complete, and the FDA can answer emergency requests for EA in 24 h (Miller et al., 2017; Holbein et al., 2015).

To conclude this bird's-eye view background, it is also important to point out that FDA EA and RTT laws are only a part of a broader set of diverse efforts to make medical products available before the completion of RCT (still considered the gold standard to assess the safety and efficacy of medical products), and/or to design different, faster methods. For example, surrogate endpoints, biomarkers or intermediate end points are increasingly used to substitute RCT and predict patient relevant outcomes (Ciani et al., 2017). In 2014, the same year of the first RTT laws, in the context of the Ebola outbreak in West Africa, the World Health Organization declared that it is ethical to offer experimental interventions, provided that certain conditions are met (World Health Organization, 2014). The Wellcome Trust (UK) has drafted guidelines to fast-track trials in humanitarian emergencies (Wellcome Trust, 2014). The USA 21st Century Cures Act (21CAA) developed in 2016 encourages the FDA to consider new evidentiary standards in the development and approval of new medical products, including data from Electronic Health Records (EHR).

1.2. Relevance of discussing RTT laws

Although RTT laws have emerged in the USA, the difficult issues they touch upon, and the complex area of end of life care in which they are situated, are relevant to other countries (Meyerson, 2017). Such issues include: the balance of therapeutic beneficence between medical research centred on the public and clinical practice centred on the individual patient; the potential conflict between individual medical autonomy and the interest of public health and medical research; the public understanding of (and trust in) the process and regulation of medical research. These issues are not only of interest to clinical, medical scientists and other experts from different disciplines such as clinical lawyers, health regulators, social scientists, and bioethicists. The increased awareness around RTT laws – also ignited by a recent popular Hollywood movie 'Dallas Buyers' Club', and by other stories of individuals who have attempted to obtain experimental treatments – means that it is likely that HCPs will deal more frequently with patients' requests for access to experimental medical products. This will particularly be the case for HCPs directly involved in the management of patients with life-threatening conditions such as cancer, infective, or neurological conditions.

1.3. Aims and outline of the paper

We aim to provide a set of ethical tools and considerations that may help to address the main issues touched by the RTT laws and their critics.

In order to illustrate the key controversies of the RTT debate, we begin by reviewing the main arguments in favour (Section 2) and against (Section 3) RTT laws. RTT advocates claim that the laws support individual autonomy by removing unnecessary and time consuming 'regulatory walls' between terminally ill patients and the experimental products which may have some therapeutic benefit. Critics have expressed concerns about the real efficacy of these laws; the nature of the 'right' they confer to patients, and how they may contribute to health inequalities. They are also concerned about the negative consequences that unregulated access to experimental medical products may have for the patient requesting access, end of life care, the sustainability of medical research and clinical trials, and for public health. In line with some literature (Lieu et al., 2015), we acknowledge that RTT laws are situated within an important debate about how to improve terminally ill patients' quality of life and decisions, but we argue that they do not provide an effective means to achieve this objective.

The issues touched by the RTT debate are very complex and blend clinical, research, and social challenges. To tackle this complexity – and to address most of the concerns of RTT advocates and its critics – we outline in Section 4, a multi-pronged approach.

First, we suggest two complementary ethical tools to improve end of

[2] We are briefly recalling only the American case, where the RTT laws have been implemented. The regulation, and terminology, for what is here called 'expanded access' varies from country to country.