New standards for evidence for evaluating regenerative medicine

Original publiction:
The Social Production of Evidence: Regenerative Medicine and the U.S. 21st Century Cures Act

Author:
Linda Hogle, Amritava Das

New laws in the US are challenging what counts as relevant evidence for approving the safety and effectiveness of new therapies. The laws promote the use of alternative forms of evidence rather than relying on conventional randomized, controlled clinical trials alone. While people in favour of the new policies argue they may speed up the approval process for regenerative medicine, provide faster access for patients and reduce barriers to translation of stem cell research, there are risks, responsibilities and biases that may come with less stringent evaluation.

What questions & challenges are raised?

Over the past few decades evidence to support the approval of new medical treatments in the United States has typically come from clinical trials and other rigorously proven methods. Randomized, controlled clinical trial data allows clinicians, researchers and governing bodies to determine whether a treatment is safe and effective, and identify possible risks and side effects before being approved. Patients have generally had limited access to unapproved treatments because there could be big risks and little, if any, benefit. However, critics argue that the evidence-based clinical trial system is slow, expensive, laborious and may be more difficult for innovative therapies such as regenerative medicine (RM). As a result, social and political pressures are leading to new policies. The 21st Century Cures Act (Cures Act) of 2016, for example, allows alternative forms of evidence to be used to approve new therapies, some of which are controversial. Critics worry that such policies may erode standards for safety and effectiveness established in the existing hypothesis-driven clinical trial system. Dr Linda Hogle from the Department of Medical History and Bioethics at the University of Wisconsin-Madison and her colleague Dr Amritava Das have written a commentary discussing this substantial shift in standards and draws parallels to other legislation, including Right-To-Try (RTT) laws aimed at increasing patients' access to unapproved medical treatments. Dr Hogle cautions that regenerative medicine has particular complexities that these new policies may not address, and that that appropriate evidence, not just expedient evidence, should be used in evaluating new treatments.

What insight & direction does this give for research policies?

In her discussion, Dr Hogle begins by pointing out that societies' definition of what counts as evidence is always changing and that, "Research governance has always been as much about power and persuasion as about matters of fact". Although there are valid reasons to consider alternative forms of evidence other than just clinical study data, the policies being adopted open up the opportunity for greater subjectivity when evaluating new therapeutics. Substantial questions remain about how much value is placed on alternative evidence, particularly with consideration to how it is collected and from whom it comes. Importantly, policy makers need to evaluate who benefits from policies that elevate alternative, observational evidence for the approval of new treatments and who will bear the risks. New policies may aim to expedite patient access to novel regenerative medicine; however, to protect patients, it is prudent to balance expediency with rigour.

What background and point are discussed?

The commentary highlights the fact that the way medical innovations are evaluated is inherently social; that is, perceptions of a need to speed innovations through approval processes or go more slowly and cautiously may be stimulated by political or economic issues as much as qualities of the innovation itself. The article recalls historical periods in the U.S. when approval processes were affected by views that regulation either needed to be more systematic and cautious or was too burdensome. The current U.S. situation of patient activism and political interest in less governmental intervention in innovation are among the conditions motivating the new policies. Dr Hogle notes that some aspects of the new laws appear to weaken established criteria for what kind and quality of evidence is considered when determining the safety and efficacy of new medical treatments. By walking the reader through several aspects of the Cures Act and RTT laws, Dr Hogle points out that these pieces of legislation permit assessment of RM treatments using new forms of data that may be beneficial in terms of lowering costs and accelerating time to approval, but are also questionable. A few kinds of evidence that the Cures Act permits for the evaluation of medical innovations include: observational data, indirect measures such as biomarker data (the presence of biological indicators suggesting that a certain biological state is present) and surrogate endpoints (indicators that may predict an outcome such as benefit or harm is achieved, rather than the actual clinical outcome itself), data from non-peer reviewed journal articles, data-mining of registries and medical records (to find patterns among patients), and associative data analytics (so-called "big data"). Parts of the Cures Act also include the use of patient-generated information to assess the impact of treatments on patients' quality of life. 'Patient experience data' and 'real-world evidence' includes documentation about how patients feel treatments are working. While such information is helpful to add to clinical data, Dr Hogle notes the subjectivity of such reports: data based upon personal accounts and experiences can be inherently biased and has similarities to testimonials used to advertise unapproved RM treatments. Also, computational methods, including associative data analytics, can handle large volumes of information quickly and relatively inexpensively, but cannot replace biological systems used to test novel treatments in the preclinical phase. There are reasons why RM treatments require careful assessment: they are very complex in nature; they often have multiple components, uncertain effectiveness, possible side effects, potentially large safety risks and unknown long-term effects. Furthermore, it is just generally difficult to prove therapies work. Careful assessment is also important because health care providers and health insurers want proof treatments work before they pay to provide them to patients. It is still not certain how treatments that are approved for use but don't have a proven effect will be provided or paid for.