CLINICAL INVESTIGATION

EDITORIAL

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How to advance medical research: less regulation, more money and more specific strategies?

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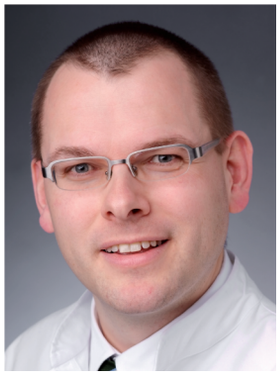

"...innovative ideas of clinicians are the motor of research. Potent research that enhances public welfare and improves prognosis and quality of life of patients frequently arises from every day clinical practice."

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Medicine has been defined as the science and art of healing. With such a broad definition, one can assume that there are multiple ways to advance medicine and medical research. A systematic approach is only possible through clinical research. In the advancement of clinical trials, downscaling of regulatory rules and upscaling of funding for clinical drug development have become the focus of current discussions. Other, more specific strategies may need to be addressed as well.

Can regulatory rules be downsized?

In the light of criticism ranging widely from scandals around manipulated data [1] to trials yielding negative results not being published [2], it is felt that strict regulation of the pharmaceutical industry is necessary. Lenient regulation for noncommercial trials seems to be an obvious incentive for academic research but implies the danger of two classes of research. It would inevitably mean lower quality in noncommercial trials, where similar scientific misconduct has been encountered [3,4].

Strict adherence to GCP guidelines is expedient and a necessary principle of clinical research to ensure first, patient safety, and second, data quality. Risks imposed on patients and data quality in a trial do not primarily depend on conflicting interests of the sponsor. Commercial interest, for example, besides from being hard to define, can be completely in line with physicians' and patients' best interests. Medical research greatly benefits from time and money invested by the pharmaceutical industry. On the other hand, sole scientific interest does not guarantee a harmless clinical trial.

Regulatory rules may need to differ, but should do so according to risk levels to relieve any unnecessary bureaucratic burden on low-risk trials. A valid distinction between risk levels would still have to be defined. For the monitoring of clinical trials, such approaches are already being developed [5].

Differing and incoherent assessments by multiple authorities or independent review boards are an example of inconsistent rather than excessive regulation posing problems in the execution of clinical trials [6].

The Clinical Trials Transformation Initiative launched by the US FDA and Duke University as an interdisciplinary consortium to modernize the way clinical trials are conducted is a promising step to free clinical research's regulatory framework of unreasonable impediments [7,101]. European regulation appears to be on the same track. According to its recent public consultation paper on the revision of the Clinical Trials Directive, the European Commission intends to cease attempts to distinguish between commercial and noncommercial sponsors and to adopt a risk-adapted approach instead [8].

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Should more money be spent on clinical research?

The responsibility of governments does not end with the definition of rules. To protect patients from harmful or ineffective treatment, and to minimize off-label use of medications and medical products, every effort needs to be made to foster independent clinical research. The execution of clinical trials is time consuming and demands special expertise, not in the least due to the elaborate regulatory requirements. Thus, clinical research becomes more and more expensive or even unaffordable if it does not meet any financial interest [9,10]. The latter kind of research inevitably needs public financial support. At the same time, public budgets are limited and have to be invested efficiently.

The only way to generate data inducing evidence is to treat a patient in a clinical trial. Funding of networks and infrastructure already exists, for example, the Clinical and Translational Science Awards [102] by the NIH, the co-funded European Clinical Research Infrastructures Network [103] and the Centers for Clinical Studies by the German Federal Ministry for Education and Research (BMBF) [104]. These structures provide the necessary basis for research. However, innovative ideas of clinicians are the motor of research. Potent research that enhances public welfare and improves prognosis and quality of life of patients frequently arises from every day clinical practice. Successful and efficient study groups and networks usually originate from trial projects, not necessarily vice versa. Consequently, sufficient public funding should follow a bottom-up approach by supporting individual trials.

The German funding program for clinical trials is an exceptional instrument to support those practical approaches to enhance patient outcome. It is executed in a unique collaboration between the German BMBF and the private German Research Foundation [105]. The program is not limited to specific fields and can therefore react to the demands of the applicants. The yearly budget has been increased from €10 to 30 million over the last 7 years. For 2010 this stated 0.001% of the gross domestic product (GDP), approximately 0.01% of total health expenditures [106,107].

Still, the essential advantage of funding by private industry is fast and efficient decision making. We urgently need a public funding system where application and review processes are conducted within weeks instead of months or years. Otherwise, independent research will always lag behind.

More specific strategies

With the special expertise needed to execute a clinical trial, there is an undeniable need to develop clinical research into a medical specialty; currently, we do not even teach clinical trials in medical school to an appropriate extent. The implicit risk of an artificial separation between research and the clinic must be overcome. Clinical research must continuously improve and update medical science, but will surely fail if it does not start before the idea for a specific clinical trial has already been born. It should be the mission of every physician specialized in any field of medicine to contribute to the enhancement of medicine. Ideally, an unmet medical need is identified while diagnosing or treating a patient. Every physician encounters unanswered clinical questions every day. The sequence should begin here, with translating the clinical question into a basic science question. From there, it should be guided back to bedside. If we focus on those interfaces we would save time and ensure translation works on a larger scale.

Discussions on clinical research usually refer to the drug development of compounds already identified or synthesized. Interestingly, the field of diagnostic tests is hardly represented in these discussions. To be able to diagnose a disease is the primary prerequisite to help patients (and clinicians). There are many diseases with established treatments, but lacking reliable and fast diagnostic tests. Examples from our field of expertise include all invasive fungal infections and many immunological disorders.

In our view, current regulations are rather sound and have the potential to lead to more reliable evidence. The additional burden caused by current regulations needs to be balanced by increased funds for clinical trials. National expenses currently spent on this purpose are too low. As a community we are still much too slow in translating basic research findings into clinical reality. The same is true for the reciprocal process.

We need reasonable regulations and adequate funds. But most of all, we need interpreters who understand both basic research and clinical demands. When these are successfully in place, true innovations will result and tax payers will support sciences that improve health.

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