Are we keeping research participants safe enough?

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Every year, millions of patients worldwide participate in randomized clinical trials in the hope of either benefiting from experimental treatments or making a difference for others needing the same type of care. But important research that could improve care for all can no longer be easily initiated and conducted in Canada.

This public good is being threatened, in part, by rules and regulations, especially for academic clinical trials where resources are limited and risks may be much less than those associated with new experimental drugs.

There is no question that research participants need protection. But regulations have grown so burdensome that they are overwhelming the very things they are meant to support and safeguard. Consequently, clinical research has been substantially decreased among industrialized countries.

For instance, in Europe, following the introduction of the amended Medicine Act in 2004, the largest cancer research network saw a drop to 7 new trials in 2005, from 38 in 2001, with an estimated 85% increase in the cost of running individual trials and an increase in the time required to start a trial.[1] The Canadian Cancer Research Alliance, a well-resourced consortium, reported a decrease of 20% in 2008 in the number of patients with cancer recruited into clinical trials.[2] These decreases in research mean that patients will have less access to new treatments.

Given that more and more research crosses national boundaries, international rules are needed to ensure that patients are kept safe and that the research is reliable — procedures to oversee and monitor clinical trials, processes to collect accurate and reliable information, and reviews of research ethics to ensure that fair and balanced information is provided to research participants during the consent process.

Current monitoring approaches are largely based on the Good Clinical Practice Guideline, several hundred pages of documents meant to protect patients involved in studies of experimental drugs with limited information on side effects.[3] The documents focus on quality assurance resulting in extensive checks and balances focused on timely and quality information.

The guideline is based on limited evidence, but it embodies the standard of research practice in most jurisdictions for all studies, including those of existing treatments, where the risks are known. As a prime example, most pharmaceutical companies and contract research organizations routinely review 100% of the case report forms against source information in the health records. These costly and time-consuming audit procedures are driving expectations by regulators for all studies, including academic studies with lower risks and far fewer resources. Worse, there is little proof that quality is improved or that patients are better protected.[3]

On another front, pharmaceutical companies and contract research organizations often compile and send hundreds, sometimes thousands, of adverse event reports to every ethics committee involved in specific studies. Aside from costly duplication of efforts, it is impossible for ethics committees to determine what the adverse events mean because they are not told whether the affected person received the experimental drug or the placebo.

Instead of developing and adopting proper, study-specific standards, we have institutionalized ineffective monitoring for all clinical research, including lower-risk academic studies. International bodies, regulatory authorities, the academic community and major granting agencies can work together to fix the system.

First, all stakeholders should undertake a synthesis of existing evidence on monitoring techniques and processes to develop proper guidelines to modernize international standards. We need a research agenda to fill knowledge gaps to support best practices for standards of monitoring and oversight of research. Such an approach would be a far better way to develop safeguards for patients involved in research.

Second, standards must be far more pragmatic and proportionate to the incremental risk imposed by individual studies. "One size fits all" will not achieve the greatest benefit for the greatest number. Minimizing all risks should not be the only guiding principle. If additional oversight is needed, it should come with additional resources from granting agencies and governments.

Third, existing oversight mechanisms should be re-evaluated. For instance, having local research ethics committees monitor major multicentre clinical trials is futile. Local committees do not have the proper authority and expertise to protect all the patients in those studies because they can only influence researchers at their institutions.

Only with appropriate expertise and access to all the research information will data monitoring and safety boards be able to determine if a study should continue or be stopped because patients are being harmed. But despite the importance of such groups, they are used arbitrarily by academic and industry studies. In addition, little guidance is offered on the criteria for their membership, expertise, reporting relationship and roles. Therefore, academic researchers can invite their friends to oversee their major study, or companies can hire researchers with whom they have longstanding relationships.

Without significant changes, our academic research enterprise — and eventually even commercial trials — will be immobilized by increasing bureaucracy and spiraling costs.

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