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EDITORIAL

Ethics in rehabilitation: challenges and opportunities to promote research

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Respecting human individuals enrolled in a trial while trying to improve the knowledge for the entire human race is not always easy but a necessary tasks. Ethics has become progressively a fundamental part of this process, with editors and publishers very committed to publish only sound and ethical research.[1] The Helsinki Declaration and its continuous updates are a pillar of ethical research.[2] However, since its statements are rather general, they must be adapted to various areas and studies in order to balance among two opposing needs for safety of human subjects and the need to discover and evaluate new treatments and their potential side effects. The Ethical Committees (EC) and the Institutional Review Boards (IRB) were born with the crucial role of balancing these different needs. Regulations were primarily developed for drugs and secondarily for surgery. As both of them can seriously harm patients, the regulations developed are quite strict.

Rehabilitation is a relatively new discipline. Its approach is markedly different from those applied in general medicine and surgery. Drugs are used only as co-treatments, and almost never represent the main standard of the rehabilitation approach. Physical medicine and exercise for functional recovery, are the main pillars of rehabilitation medicine, together with orthoses and prosthesis that are widely used.[3-4] Therefore, research in the field of rehabilitation can have difficultly navigating through the complex system and managing regulatory needs that have not been optimally adapted to the rehabilitation field.

Institutional Review Board and Ethical Committees

The IRB in the USA and the EC in Europe are responsible for reviewing and approving all human trials, and today this approval is a pre-requisite for every article submission in the most of journals.[6] These boards have the task of assigning levels of risks of study. For the US risks are assessed by categories including: exempt from review, no greater than minimal risk, and greater than minimal risk (Figure 1).[7]

For Europe, the review process is not standardized among different countries, and in the same country, there are differences in management among the EC in different cities or regions. The legislator considers only one main distinction: observational studies, in which the patients included will undergo a standard and labeled treatment independently from their inclusion or exclusion from the study, and experimental studies. In the first case, the EC approves or disapproves after reading a short project, with no need for convocation of the responsible researcher. In case of very low-risk studies, a simple notification is required, but the EC can ask for more details and suggest changes in the protocol before approving or disapproving it formally. The prospective observational studies represent and exception and convocation is usually required, as it happens in all experimental studies (Figure 2). If the EC disapproves a project, the faculty of the EC will decide whether to allow the investigator to re-submit or not. Whatever happens, this procedure is time consuming for researchers.

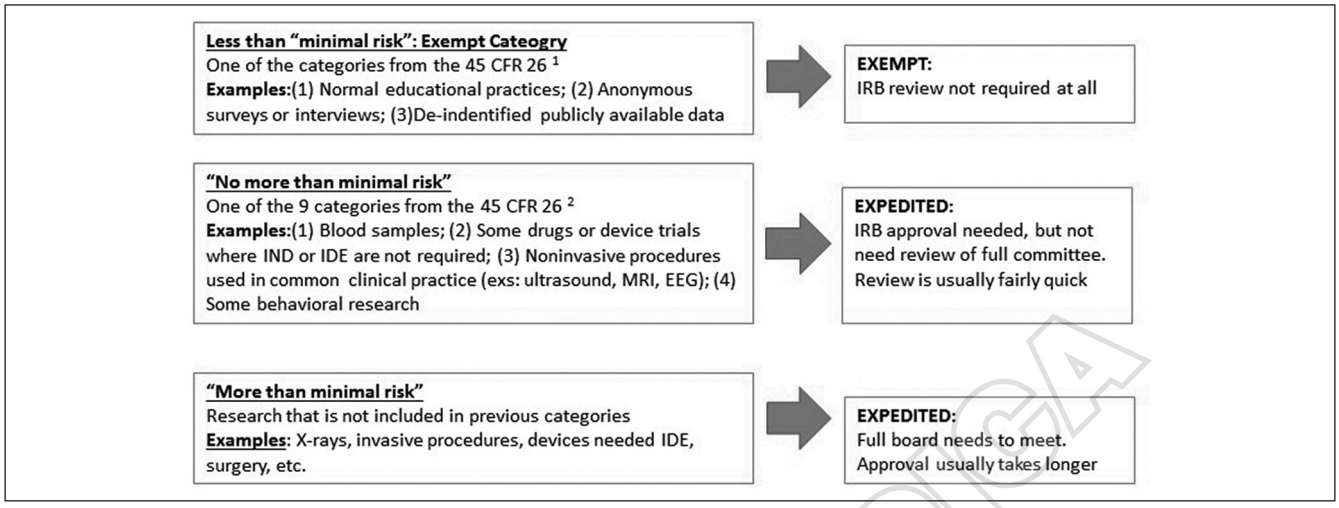

Figure 1.—IRB Level of Risks and Types of Review needed.[7]

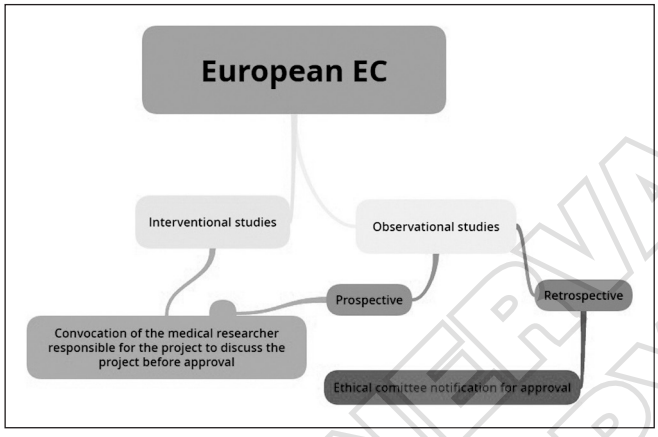

Figure 2.—Functioning of the Ethical Committee in Europe.

Researchers need to be aware of the assessed risk level of the study in order also to design appropriate safety measurements in the trial. For instance, when the risk assessment is high, the IRB/EC may determine that only few patients are tested or also determine that a more constant assessment and report is made in order to monitor closely such studies.

Challenges of regulatory systems

An important role of IRB/EC is to assess that the planned trial is methodologically correct, especially for observational studies as they lack randomization, which may introduce bias into the study. The IRB/EC have to check the research question, the outcomes, and analysis chosen.

One of the challenges for the IRB/EC is to determine the appropriate risk level, since frequently experts in the field are not included in these boards as it is not possible to have experts for the wide range of scientific topics in rehabilitation. Therefore, IRB/EC may sometimes under or overestimate risk levels in a study, thus requesting inadequate safety measurements. Although many studies in the rehabilitation field fall into the category of "no greater than minimal risk", there is still a significant burden to the investigator that may be the result also of inadequate training of the investigator in the IRB process.

Due to this complex regulatory system, the effort for conducting research in rehabilitation may fail to due lack of resources, resulting in a lack of clinical trials. The problem of the scarcity of research in the field is compounded by the fact that research is commonly not integrated with clinical care. For example, the Tecar therapy (Resistive Capacitive Energy Transfer — a therapy based on the electric condenser principle), commonly clinically used, according to a PubMed search (March 1st, 2016), only produced four results for research articles (Figure 3). If more clinical practices were involved in research, even simpler studies such as observational studies could help to determine the risk and effectiveness of this therapy.

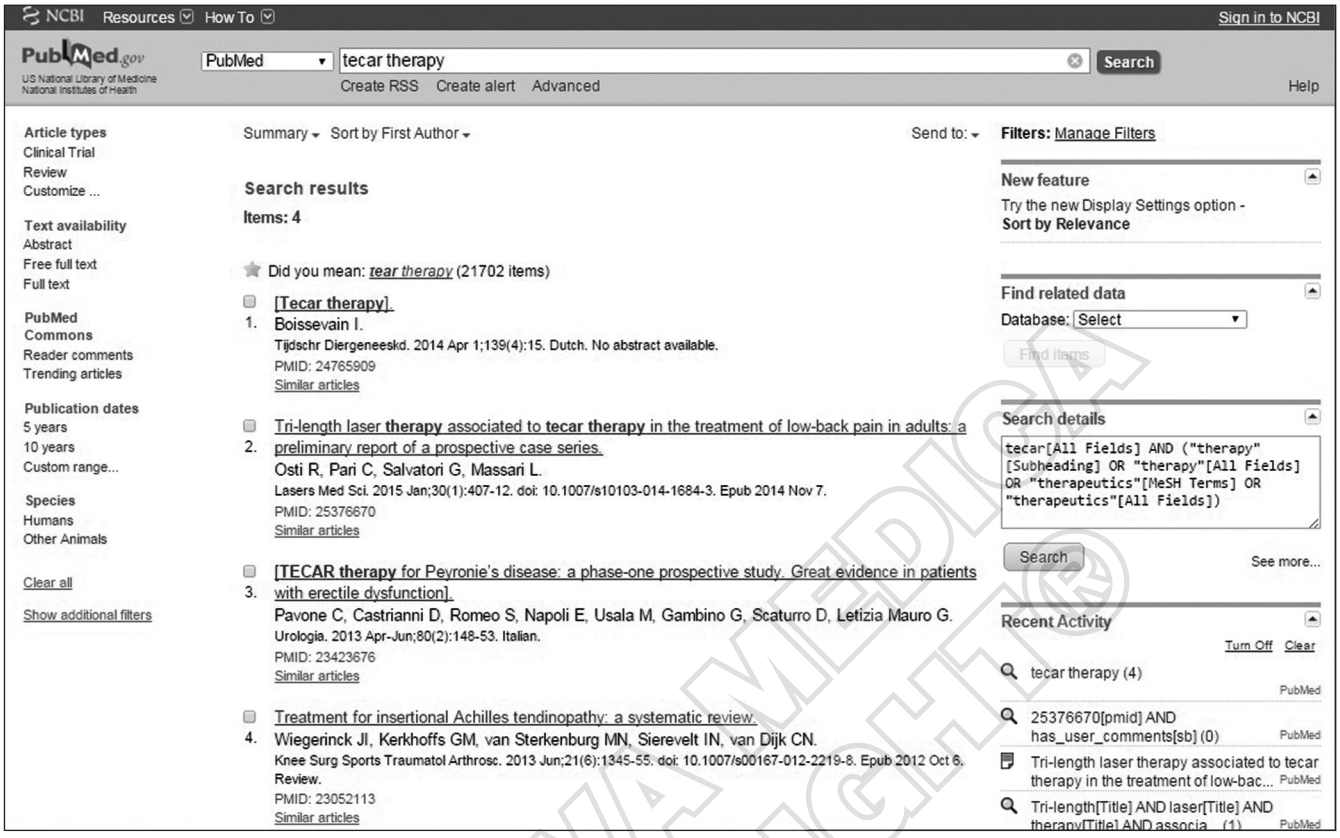

Figure 3.—Medline search for Tecar therapy.

Recommendations moving forward

We strongly believe that a new ethical approach and regulation should develop in order to fit the needs of the rehabilitation field and also to promote further research in this field, like proposed in other fields.

Enhancing regulatory training among rehabilitation researchers and clinicians

Promoting better and more interactive courses in regulations for rehabilitation researchers and clinicians would have a positive impact in two aspects: providing trained personnel to participate in IRB/EC and enhancing research to decrease the amount of work for a protocol to be approved. One of the main requirement for a trial to be approved by IRB/EC is a good methodology of the research project, and therefore this training will enhance the quality of submitted projects, in agreement with ethical requirements.[8].

Developing guidelines to help with risk assessment

Another way could be based on tables of risks or score checklist that consider both the study design, the pathology, and the treatment in order to assign almost automatically a risk level and simplify the related steps in the ethical assessment. This risk level should help institutions to designate the appropriate level of review and requirements. The simplification of the procedure will finally allow a guide for IRB/EC evaluation, by making the procedures more homogeneous among different countries.

Designing studies with decreased risk level such as observational studies

In addition, to conduct more observational studies to get preliminary data about the efficacy of rehabilitation. These studies might be more achievable for researchers with limited researchers, as researchers can consent

subjects who are already participating in a rehabilitative intervention anyways.

Another option is retrospective studies. For relatively simple retrospective studies Stefansson et al. proposed that individual medical researchers may be licensed by IRB/EC to perform retrospective clinical studies at their institution in a specific field of medicine.[9] The license would be dependent on their knowledge, expertise, and acceptance of a code of ethics. The researchers may provide copies of scientific reports that have been submitted to medical journals to allow the IRB/EC to check manuscripts for possible violations of ethical rules and potentially to prevent publication. A violation of ethical rules may result in the medical researcher losing his/her license to conduct clinical studies. Another practical proposal, by the same authors is that IRB/EC simplify approval procedures for retrospective clinical research projects, *e.g*. by a type of web-based 'fast track' response.

Conclusions

As ethical principles are fundamental in research, the IRB/EC procedures are indeed intended to protect the individual who is contributing to promote new knowledge. Nevertheless, we think it is time to develop better training of regulatory systems to the researchers and also physicians. This training needs to be also customized to the rehabilitation field. This training would improve research output, decrease IRBs and ECs overload, and improve the relationship between IRB/EC with investigators. There is a relatively urgent need to improve interventions in rehabilitation. Reviewing and optimizing the regulatory system among rehabilitation researchers may help with this important task.

References

1. Committee on Publication Ethics: COPE | Raising the Quality of Academic Journals [Internet]. Available from: http://publicationethics.org/ [cited 2016 May 4].
2. WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects [Internet]. 2013. Available from: http://www.wma.net/en/30publications/10policies/b3/ [cited 2016 May 4].
3. Negrini S, Minozzi S, Taricco M, Ziliani V, Zaina F. A systematic review of physical and rehabilitation medicine topics as developed by the Cochrane Collaboration. Eur Medicophysica 2007;43:381-90.
4. Negrini S. An outstanding first Impact Factor of 2.246 for the European Journal of Physical and Rehabilitation Medicine, Official Journal of SIMFER, ESPRM, and MFPMR, and now also published "in association with" ISPRM. Eur J Phys Rehabil Med 2011;47:355-8.
5. Negrini S. Behind the curtain of the European journal of physical and rehabilitation medicine: internal audit, impact factor, and more. Eur J Phys Rehabil Med 2010;46:117-23.
6. ICMJE | Recommendations [Internet]. Available from: http://www.icmje.org/recommendations/ [cited 2016 May 4].
7. US Health and Human Services. OHRP Expedited Review Categories; 1998 [Internet]. Available from: www.hhs.gov/ohrp/regulations-and-policy/guidance/categories-of-research-expedited-review-procedure-1998/index.html [cited 2016 May 4].
8. Suemoto CK, Ismail S, Corrêa PCRP, Khawaja F, Jerves T, Pesantez L, *et al*. Five-year review of an international clinical research-training program. Adv Med Educ Pract 2015;6:249-57.
9. Stefánsson E, Atladóttir ÓY, Guðbjörnsson B. Are ethics rules too strict in retrospective clinical studies? Acta Ophthalmol (Copenh) 2008;86(6):588-90.

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