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Balkan Clinical Research Registry: Established by Academy of Medical Sciences of Bosnia and Herzegovina

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ABSTRACT

Background: From 2013 the World Medical Association's Declaration of Helsinki explicitly requires pre-registration of a study involving human subjects. The registration gives a chance for improvement of design and avoidance of bias. **Objective:** The aim of this article was to describe process of bearing decision to create regional registry of clinical studies for Balkan countries. **Methods:** After finding relevant studies about research registries and designing the concept and structure of future regional registry an article was published in IJBH journal. The article was then used as basis for discussion at 2020 meeting of Academy of Medical Sciences of Bosnia and Herzegovina (AMSBH), and final decision was made by the Academy to create the research registry. **Results:** Regional registry of clinical studies will be under the auspices of AMSBH and web-based, with the option of online registration of new studies. The data required to be entered in the moment of registration relate to key elements of research plan: topic, variables, sample, type of the study and the study population. After applying for registration of a clinical study, the authors will soon receive the review made by the AMSBH expert committee. The application could be accepted, rejected or returned for major or minor revision. After an application is accepted, it will be deposited in the searchable database and given the registration number. **Conclusion:** The AMSBH's decision to create the regional registry of clinical studies will satisfy needs of researchers from Balkan countries in the first place, who share cultural and lingual similarities. It will also help with increasing standards of clinical research in the region.

Keywords: Clinical study; Registry; Risk of bias; Transparency.

1. INTRODUCTION

Registering a study involving human subjects before its onset is a requirement recently imposed by the World Medical Association's Declaration of Helsinki – Ethical Principles for Medical Research involving Human Subjects, version 2013 (1). In the article 35 of this declaration is explicitly demanded: „Every research study involving human subjects must be registered in a publicly accessible database before recruitment of the first subject.“ There are several clinical research registries that operate on a global level: the „ClinicalTrials.gov“ database of US National Institute of Health (2); the World Health Organization's register of clinical trials entitled „International Clinical Trials Registry Platform“ (ICTRP) in 2005 (3); PROSPERO database of systematic reviews and meta-analyses, by University of York Centre for Reviews and Dissemination, United Kingdom (4), the Cochrane Database of Systematic reviews (5); and the Research Registry (6).

Main reason for registering a clinical study protocol before initiation of the study is transparency: anyone interested should have access to the protocol and check methodology issues. It is methodology of a study that reflects its quality; only if basic research principles are fully implemented in the study design, a reader may trust to the results obtained. Therefore, the first benefit of registering and making study protocols visible to everybody is ensurance

DISCLAIMER: “This article is updated version of the publication Masic I, Jankovic MS. Why Registering Your Research Study Involving Human Subjects Before Its Onset? Int J Biomed Healthc. 2020; 8(2): 64-67. doi: 10.5455/ijbh.2020.8.64-67, as it was adopted on the annual meeting of Academy of Medical Sciences of Bosnia and Herzegovina, held in Sarajevo, on November the 14th, 2020. Although there are some substantial changes, majority of the text is the same as in the primary publication from IJBH.

of sufficient methodological quality, which is achieved by review and revisions of the protocols prior to their registration and publication (7). Second, other investigators within the same field may become aware of ongoing studies and avoid duplicating the same design. Third, the results that will be published in future could be matched to original study design, and any discrepancies or post-hoc manipulations revealed. Finally, if results of the registered studies are added to the records after their completion, even if they are not published in a journal, they will be accessible to research community; it is especially important for studies with negative results, i.e. where difference among the study groups was not significant, since majority of medical journals avoid publication of such results.

2. IMPORTANCE OF HAVING REGIONAL REGISTRIES

Although several registries for pre-registration of studies involving human subjects already exist on global level, there are certain weaknesses derived from their global character. If a registry accepts studies from all over the world, inevitably number of registrations will be large and will grow exponentially (e.g. Research Registry after only five years of functioning has more than 5000 registrations) (8); if founders of the registry are not having sufficient funds to heavily invest in peer review of the submitted study protocols, the registration may become purely formal and lose its intended benefits. Another weakness is limited amount of information about the registrants which depend on her/his frankness and honesty; without knowledge about the research context and state-of-art in healthcare and research milieu where the study proposal comes from, it is difficult to recognize methodological errors, research misconduct or possible ethical issues.

Regional or national research registries were established in a number of cases, and their functioning was associated with improvement in both quantity and quality of clinical research within the areas covered. Researchers rapidly became aware of regional registries, and majority complied well with requirements and standards of registering clinical studies, although periodic audits are still necessary for full adherence (9). National registries of clinical studies were established in Japan back in 2005 (10), in Sri Lanka in 2010 (11), South Korea (Clinical Research Information Service), and many other countries, while regional registry of clinical trials was founded in European Union (European Clinical Trials Registry (EuCTR)) (12). It is interesting that small national registries performed better than large international ones: the registrations were more frequently complete in small registries, and researchers were more aware of national or regional registries than of international ones (11).

Researchers in Balkan countries are even less aware of international registries involving clinical studies, and of Helsinki declaration's recommendation that all studies on human subjects should be registered prior to enrollment of the first patient. Recent survey of transpar-

ency and visibility of clinical trials in Croatia (13) was concentrated on potential users of reports registered at previously mentioned international registers of clinical investigations. It showed that, although registered in international registries, they are not visible to patients and probably to researchers that work on other types of clinical studies, apart from randomized clinical trials. The importance of visibility of ongoing clinical trials or studies in general for patients who are potential study subjects could not be overestimated. Recruiting sufficient number of study participants is not an easy task even when disorders that are studied occur with high frequency in general population (e.g. asthma or diabetes

Title of the research project	
The study acronym	
Principal investigator and his (her) affiliation	
List of other investigators with e-mails and affiliations	
Sponsor of the study, if any:	
Study design (underline the applicable)	Interventional study
	Cohort study
	Cross/sectional study
	Case/control study
	Meta-analysis or systematic review
Qualitative study	
Study design – further specification, if applicable (e.g. double-blind, randomized, controlled clinical trial, nested case/control study, etc.)	
Time and place of the study conduct	
Study population (inclusion, non-inclusion and exclusion criteria)	
Size of the study sample (calculation method, inputs and result)	
Sampling method (random, convenience, etc.)	
Methods of literature search (for meta-analyses and systematic reviews only)	Who will perform the search When Source databases Search strategy
Primary outcome of the study	
Secondary outcomes of the study	
Presumed independent variables	
Confounders	
Planned statistical processing	
Ethics committee or Investigation research Board that will evaluate the study	
Funding source, if any	
Measures for controlling bias	
What novelty will the study bring?	
Could results be applied (generalized) to other populations or patient groups?	
How the results will affect health-care?	

Table 1. The clinical study registration form.

mellitus), and it becomes very difficult when a disease studied is rare or associated with impairment of consciousness or cognition. Clinical trials are mostly done in tertiary care health facilities with limited number of beds and staff that is already engaged in other activities. In the same time there are dozens of ongoing trials, so it is of vital importance that potential participants know what studies are active and where they could be enrolled to receive an investigational, but potentially curable treatment.

There are several reasons why researchers should be well acquainted with ongoing and completed clinical investigations. The first is to avoid unnecessary duplication of research efforts, and to modify own study protocol maintaining novelty of potential findings. The second reason is potential of collaboration with investigators of already ongoing studies: clinicians may want to include their regular healthcare patients in such studies, in order to receive promising investigational drugs, especially if all standard therapeutic options are exhausted. Third issue is help when designing new study within the same therapeutic area as already registered trial. It is extremely useful to read through data of registered studies and get an insight in outcomes worthy of following and variables of significance that should be taken into account. Choice of study groups and statistical tests is also crucial, and registered studies may offer important suggestions.

In general, Foundation and successful operation of a registry of clinical studies only for Balkan region would be of great help to regional researchers, giving them chance not only to register their research, but also to improve it through preregistration peer review and useful advices how to avoid bias and methodological errors (14, 15).

3. DECISION OF AMSBH TO ESTABLISH BALKAN CLINICAL RESEARCH REGISTRY (BCRR)

After one-day meeting in Sarajevo, on Saturday the 14th, 2020, members of the AMSBH unanimously agreed that regional clinical research registry for Balkan countries (entitled “Balkan Clinical Research Registry”, or BCRR) should be established under the auspices of the AMSBH, which is respectful regional scientific organization, open to everyone in the region and independent from financial and political power centers (16).

The Academy of Medical Sciences of Bosnia and Herzegovina (AMSBH) has high scientific standards, and is open to all countries within the Balkan region. The AMSBH decided to create electronic form of the registry on a reliable server with suitable web-page that will include registration forms, necessary instructions and other information important for applicants.

Modus operandi of the BCRR should follow the algorithm described at Figure 1. The AMSBH assembly

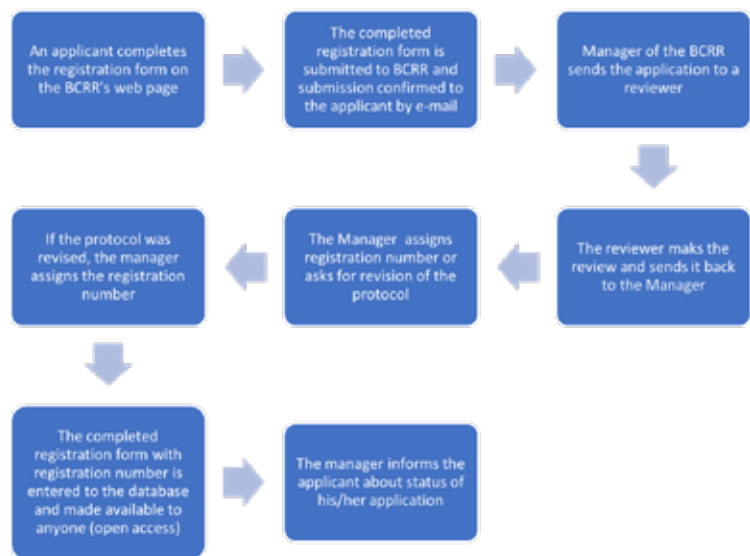


Figure 1. Algorithm describing functioning of the BCRR.

adopted the version of the registration form shown in the Table 1.

4. CONCLUSION

Pre-registration of clinical studies increase transparency of methodological issues and creates an opportunity to improve design and decrease risk of bias. Although there are numerous international registries, the newly founded regional registry of clinical studies for Balkan countries (Balkan Clinical Research Registry) would suit well the whole region, considering great socio-economic, cultural and lingual similarities of the Balkan countries.

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- **Conflict of interest:** None declared
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